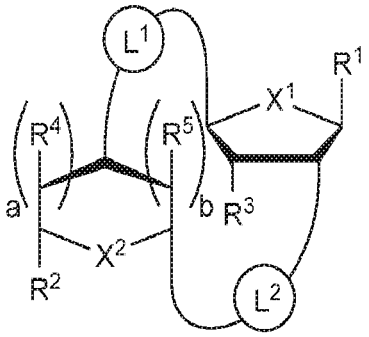
**CLAIMS:**

1. A compound of Formula **Ia**, or a pharmaceutically acceptable salt thereof,

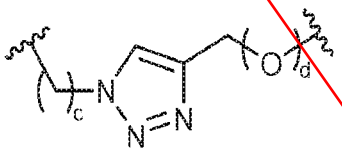
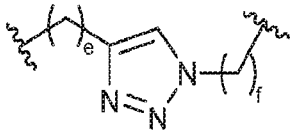


Formula **Ia**

wherein:

a and b are independently 0 or 1 and a + b = 1, when a is 1, b is 0 and $R^5$ is not present; and when a is 0, b is 1 and $R^4$ is not present;

$X^1$ and $X^2$ are independently O, S or Se in a five-membered ring;

$L^1$, starting from the carbon alpha to $X^1$, and $L^2$, starting from the carbon alpha to $X^2$, are independently -$CH_2$O-P(O)$R^6$-O-,-$CH_2$O-P(S)$R^6$-O-, -C($Y^1$)($Y^2$)O-P(O)$R^6$-C($Y^3$)($Y^4$)-, -$CH_2NHSO_2NH$-, -$CH_2NHC(O)NH$-, -$CH_2NHC(S)NH$-, -$CH_2NHC(NH)NH$-, -$CH_2NHC(O)CH_2$-, -$CH_2NHSO_2CH_2$-, -$CH_2CH_2C(O)NH$-, -$CH_2CH_2SO_2NH$-, -$CH_2NH$(3,4-dioxocyclobuten-1,2-diyl)NH-,  , or  ;

c is 0, 1, or 2;

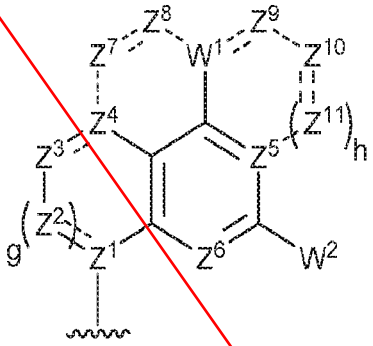
d, e, and f are independently 0 or 1;

$Y^1$, $Y^2$, $Y^3$, and $Y^4$ are independently H or F;

$R^6$ is hydroxyl, thiol, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), borano (-$BH_3^-$), or -$NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, cyclic -($C_{1-6}$alkyl)-, cyclic -($C_{1-6}$alkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups, cyclic -($C_{1-6}$oxaalkyl)-, or cyclic -($C_{1-6}$oxaalkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;

$R^1$ and $R^2$ are independently aromatic rings or heteroaromatic rings with the following general structure including its tautomeric forms:




g and h are independently 0 or 1;

$W^1$ and $W^2$ are independently hydrogen, halogen, hydroxyl, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or -$NR^7R^8$;

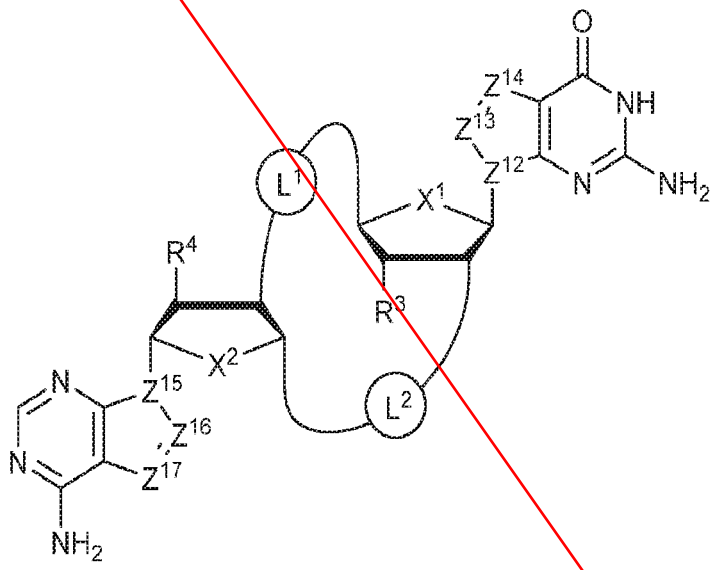
$Z^1$, $Z^2$, $Z^3$, $Z^4$, $Z^5$, and $Z^6$ are independently CH or N;

if present, $Z^7$, $Z^8$, $Z^9$, $Z^{10}$, and $Z^{11}$ are independently CH or N, and then $W^1$ is CH or N;

$R^3$, $R^4$, and $R^5$ are independently hydrogen, halogen, hydroxyl, amino, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or -$NR^7R^8$; and

the compound is not 2'3'-cGAMP.

2. The compound of claim 1 wherein the compound of Formula **IIb**, or a pharmaceutically acceptable salt thereof,

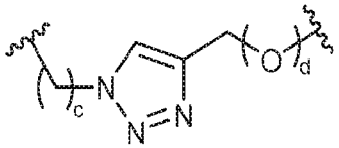
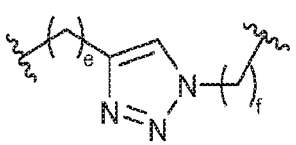


Formula **IIb**

wherein:

$X^1$ and $X^2$ are independently O, S or Se;

$Z^{12}$, $Z^{13}$, $Z^{14}$, $Z^{15}$, $Z^{16}$, and $Z^{17}$ are independently CH or N;

$L^1$, starting from the carbon alpha to $X^1$, and $L^2$, starting from the carbon alpha to $X^2$, are independently -$CH_2O$-P(O)$R^6$-O-,-$CH_2O$-P(S)$R^6$-O-, -$C(Y^1)(Y^2)$O-P(O)$R^6$-$C(Y^3)(Y^4)$-, -$CH_2NHSO_2NH$-, -$CH_2NHC(O)NH$-, -$CH_2NHC(S)NH$-, -$CH_2NHC(NH)NH$-, -$CH_2NHC(O)CH_2$-, -$CH_2NHSO_2CH_2$-, -$CH_2CH_2C(O)NH$-, -$CH_2CH_2SO_2NH$-, -$CH_2NH$(3,4-dioxocyclobuten-1,2-diyl)NH-,  , or  ;

c is 0, 1, or 2;

d, e, and f are independently 0 or 1;

$Y^1$, $Y^2$, $Y^3$, and $Y^4$ are independently H or F;

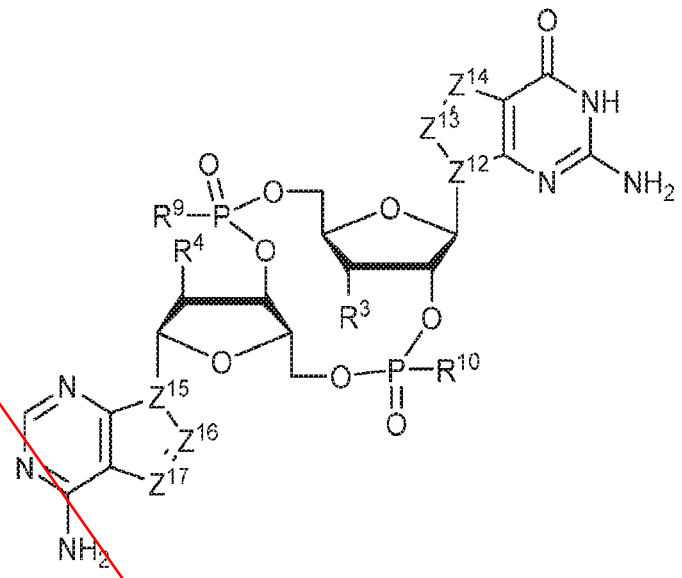
$R^6$ is hydroxyl, thiol, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), borano (-$BH_3^-$), or -$NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, cyclic -($C_{1-6}$alkyl)-, cyclic -($C_{1-6}$alkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups, cyclic -($C_{1-6}$oxaalkyl)-, or cyclic -($C_{1-6}$oxaalkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;

$R^3$ and $R^4$ are independently hydrogen, halogen, hydroxyl, amino, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or -$NR^7R^8$; and

the compound is not a previously disclosed compound, including 2'3'-cGAMP.

3. The compound of claim 1, wherein a compound of Formula **Ic**, or a pharmaceutically acceptable salt thereof,



Formula **Ic**

wherein:

$Z^{12}$, $Z^{13}$, $Z^{14}$, $Z^{15}$, $Z^{16}$, and $Z^{17}$ are independently CH or N;

$R^3$ and $R^4$ are independently hydrogen, halogen, hydroxyl, amino, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or $-NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, cyclic -($C_{1-6}$alkyl)-, cyclic -($C_{1-6}$alkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups, cyclic -($C_{1-6}$oxaalkyl)-, or cyclic -($C_{1-6}$oxaalkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;

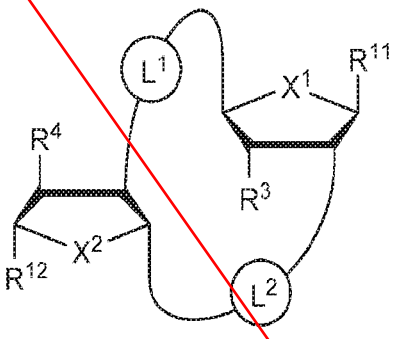
$R^9$ and $R^{10}$ are independently hydroxyl, thiol, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl,

$C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), borano ($-BH_3^-$), or $-NR^7R^8$;

the oxygen atom in one or both of the tetrahydrofuranyl rings of Formula **Ic** can be optionally replaced by a sulfur or a selenium atom; and

the compound is not 2'3'-cGAMP.

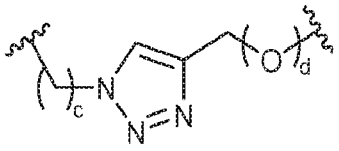
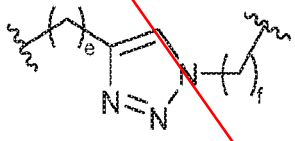
4. The compound of claim 1, wherein a compound of Formula **Id**, or a pharmaceutically acceptable salt thereof,




Formula **Id**

wherein:

$X^1$ and $X^2$ are independently O, S or Se;

$L^1$, starting from the carbon alpha to $X^1$, and $L^2$, starting from the carbon alpha to $X^2$, are independently $-CH_2O-P(O)R^6-O-$, $-CH_2O-P(S)R^6-O-$, $-C(Y^1)(Y^2)O-P(O)R^6-C(Y^3)(Y^4)-$, $-CH_2NHSO_2NH-$, $-CH_2NHC(O)NH-$, $-CH_2NHC(S)NH-$, $-CH_2NHC(NH)NH-$, $-CH_2NHC(O)CH_2-$, $-CH_2NHSO_2CH_2-$, $-CH_2CH_2C(O)NH-$, $-CH_2CH_2SO_2NH-$, $-CH_2NH$(3,4-dioxocyclobuten-1,2-diyl)NH-,  , or  ;



c is 0, 1, or 2;

d, e, and f are independently 0 or 1;

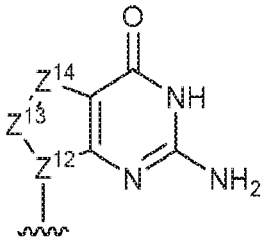
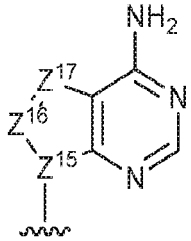
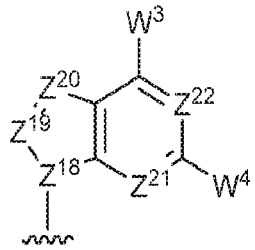
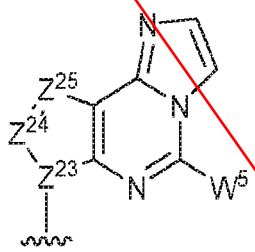
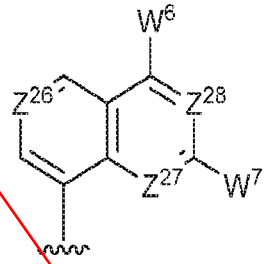
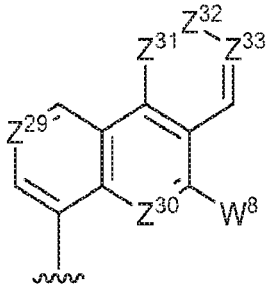
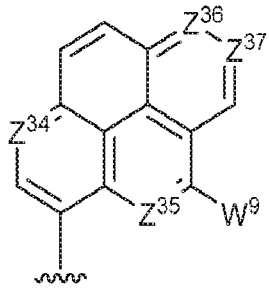
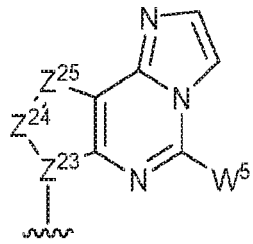
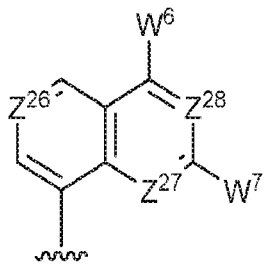
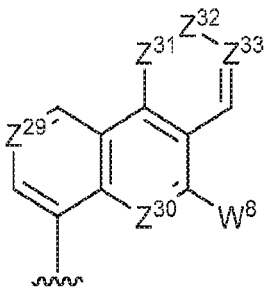
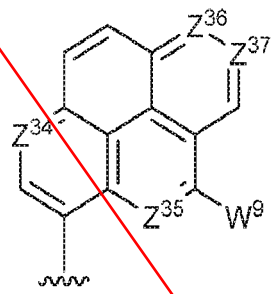
$Y^1$, $Y^2$, $Y^3$, and $Y^4$ are independently H or F;

$R^6$ is hydroxyl, thiol, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), borano ($-BH_3^-$), or $-NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, cyclic -($C_{1-6}$alkyl)-, cyclic -($C_{1-6}$alkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups, cyclic -($C_{1-60}$oxaalkyl)-, or cyclic -($C_{1-60}$oxaalkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;

$R^3$ and $R^4$ are independently hydrogen, halogen, hydroxyl, amino, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or $-NR^7R^8$;

$R^{11}$ and $R^{12}$ are independently selected from the group consisting of:

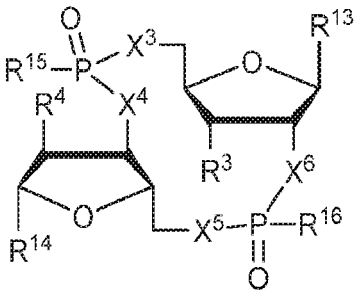












, with at least one of $R^{11}$ and $R^{12}$ being , , , , , or ;

$Z^{12}$, $Z^{13}$, $Z^{14}$, $Z^{15}$, $Z^{16}$, $Z^{17}$, $Z^{18}$, $Z^{19}$, $Z^{20}$, $Z^{21}$, $Z^{22}$, $Z^{23}$, $Z^{24}$, $Z^{25}$, $Z^{26}$, $Z^{27}$, $Z^{28}$, $Z^{29}$, $Z^{30}$, $Z^{31}$, $Z^{32}$, $Z^{33}$, $Z^{34}$, $Z^{35}$, $Z^{36}$, and $Z^{37}$ are each independently CH or N; and

$W^3$, $W^4$, $W^5$, $W^6$, $W^7$, $W^8$, and $W^9$ are independently hydrogen, halogen, hydroxyl, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or $-NR^7R^8$.

5. The compound of claim 1, wherein a compound of Formula **Ie**, or a pharmaceutically acceptable salt thereof,

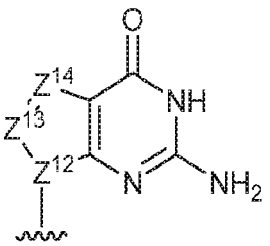


Formula **Ie**

wherein:

$X^3$, $X^4$, $X^5$, and $X^6$ are independently O, NH, $CH_2$, CHF, or $CF_2$;

$R^{13}$ and $R^{14}$ are independently selected from the group consisting of:



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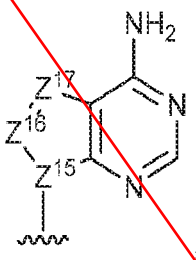

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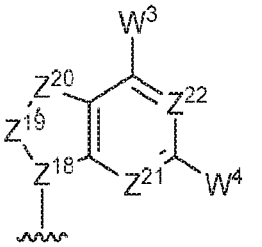

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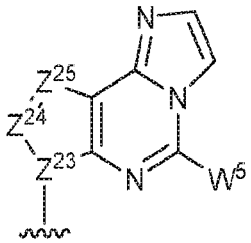
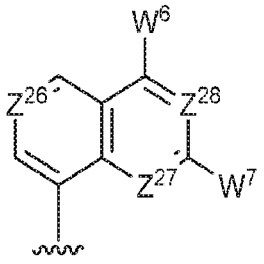


, and



,

$Z^{12}$, $Z^{13}$, $Z^{14}$, $Z^{15}$, $Z^{16}$, $Z^{17}$, $Z^{18}$, $Z^{19}$, $Z^{20}$, $Z^{21}$, $Z^{22}$, $Z^{23}$, $Z^{24}$, $Z^{25}$, $Z^{26}$, $Z^{27}$, and $Z^{28}$ are each independently CH or N; and

$W^3$, $W^4$, $W^5$, $W^6$, and $W^7$ are independently hydrogen, halogen, hydroxyl, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or -$NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, cyclic -($C_{1-6}$alkyl)-, cyclic -($C_{1-6}$alkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups, cyclic -($C_{1-6}$oxaalkyl)-, or cyclic -($C_{1-6}$oxaalkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;

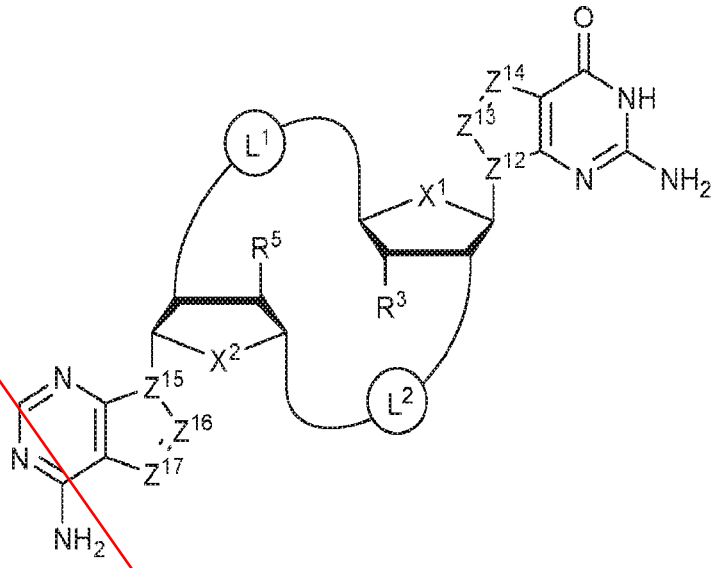
$R^3$ and $R^4$ are independently hydrogen, halogen, hydroxyl, amino, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or -$NR^7R^8$;

$R^{15}$ and $R^{16}$ are independently hydroxyl, thiol, methoxy, ethoxy, amino, *N*-methylamino, *N*,*N*-dimethylamino, *N*-ethylamino, *N*,*N*-diethylamino, *N*-morpholino, or borano (-$BH_3^-$);

the oxygen atom in one or both of the tetrahydrofuranyl rings of Formula **Ie** can be optionally replaced by a sulfur or a selenium atom; and

the compound is not 2'3'-cGAMP.

6. The compound of claim 1, wherein a compound of Formula **If**, or a pharmaceutically acceptable salt thereof,

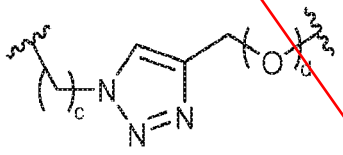
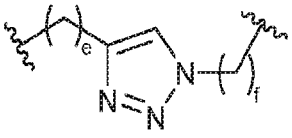


Formula **If**

wherein:

$X^1$ and $X^2$ are independently O, S or Se;

$Z^{12}$, $Z^{13}$, $Z^{14}$, $Z^{15}$, $Z^{16}$, and $Z^{17}$ are independently CH or N;

$L^1$, starting from the carbon alpha to $X^1$, and $L^2$, starting from the carbon alpha to $X^2$, are independently -$CH_2O$-P(O)$R^6$-O-,-$CH_2O$-P(S)$R^6$-O-, -C($Y^1$)($Y^2$)O-P(O)$R^6$-C($Y^3$)($Y^4$)-, -$CH_2NHSO_2NH$-, -$CH_2NHC(O)NH$-, -$CH_2NHC(S)NH$-, -$CH_2NHC(NH)NH$-, -$CH_2NHC(O)CH_2$-, -$CH_2NHSO_2CH_2$-, -$CH_2CH_2C(O)NH$-, -$CH_2CH_2SO_2NH$-, -$CH_2NH$(3,4-dioxocyclobuten-1,2-diyl)NH-,  , or  ;

c is 0, 1, or 2;

d, e, and f are independently 0 or 1;

$Y^1$, $Y^2$, $Y^3$, and $Y^4$ are independently H or F;

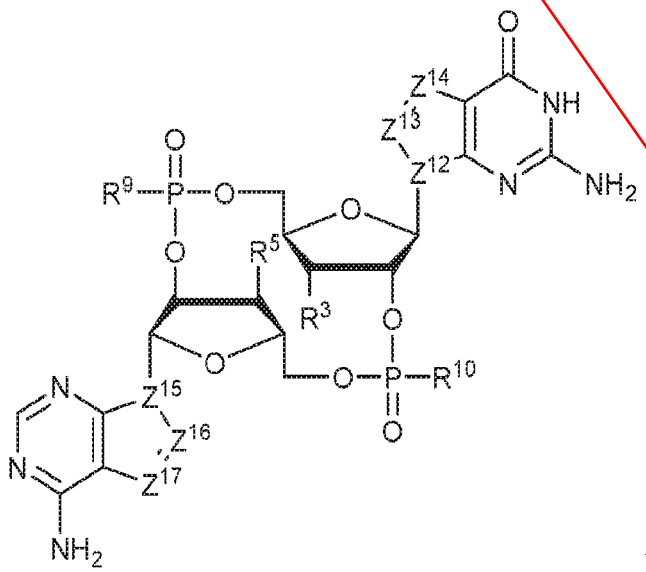
$R^6$ is hydroxyl, thiol, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), borano (-$BH_3^-$), or -$NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, cyclic -($C_{1-6}$alkyl)-, cyclic -($C_{1-6}$alkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups, cyclic -($C_{1-6}$oxaalkyl)-, or cyclic -($C_{1-6}$oxaalkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;

$R^3$ and $R^5$ are independently hydrogen, halogen, hydroxyl, amino, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or -$NR^7R^8$; and

the compound is not 2'2'-cGAMP.

7. The compound of claim 1, wherein a compound of Formula **Ig**, or a pharmaceutically acceptable salt thereof,



Formula **Ig**

wherein:

$Z^{12}$, $Z^{13}$, $Z^{14}$, $Z^{15}$, $Z^{16}$, and $Z^{17}$ are independently CH or N;

$R^3$ and $R^5$ are independently hydrogen, halogen, hydroxyl, amino, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or -$NR^7R^8$;

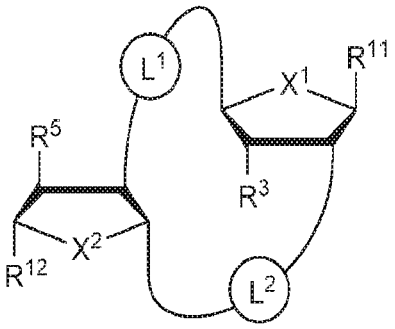
$R^7$ and $R^8$ are independently hydrogen, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, cyclic -($C_{1-6}$alkyl)-, cyclic -($C_{1-6}$alkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups, cyclic -($C_{1-6}$oxaalkyl)-, or cyclic -($C_{1-6}$oxaalkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;

$R^9$ and $R^{10}$ are independently hydroxyl, thiol, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), borano (-$BH_3^-$), or -$NR^7R^8$;

the oxygen atom in one or both of the tetrahydrofuranyl rings of Formula **Ig** can be optionally replaced by a sulfur or a selenium atom; and

the compound is not 2'2'-cGAMP.

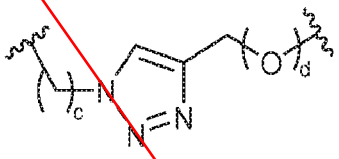
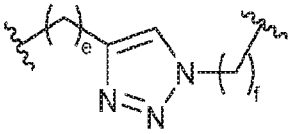
8. The compound of claim 1, wherein a compound of Formula **Ih**, or a pharmaceutically acceptable salt thereof,




Formula **Ih**

wherein:

$X^1$ and $X^2$ are independently O, S or Se;

$L^1$, starting from the carbon alpha to $X^1$, and $L^2$, starting from the carbon alpha to $X^2$, are independently -$CH_2O$-P(O)$R^6$-O-,-$CH_2O$-P(S)$R^6$-O-, -C($Y^1$)($Y^2$)O-P(O)$R^6$-C($Y^3$)($Y^4$)-, -$CH_2NHSO_2NH$-, -$CH_2NHC(O)NH$-, -$CH_2NHC(S)NH$-, -$CH_2NHC(NH)NH$-, -$CH_2NHC(O)CH_2$-, -$CH_2NHSO_2CH_2$-, -$CH_2CH_2C(O)NH$-, -$CH_2CH_2SO_2NH$-, -$CH_2NH$(3,4-dioxocyclobuten-1,2-diyl)NH-,  , or  ;

c is 0, 1, or 2;

d, e, and f are independently 0 or 1;

$Y^1$, $Y^2$, $Y^3$, and $Y^4$ are independently H or F;

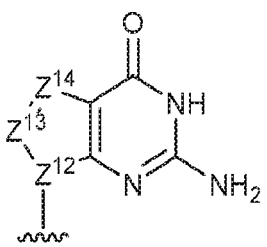
$R^6$ is hydroxyl, thiol, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), borano (-$BH_3^-$), or -$NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, cyclic -($C_{1-6}$alkyl)-, cyclic -($C_{1-6}$alkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl,

carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups, cyclic -($C_{1-6}$oxaalkyl)-, or cyclic -($C_{1-6}$oxaalkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;

$R^3$ and $R^5$ are independently hydrogen, halogen, hydroxyl, amino, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or $-NR^7R^8$;

$R^{11}$ and $R^{12}$ are independently selected from the group consisting of:



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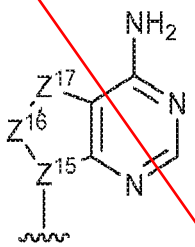

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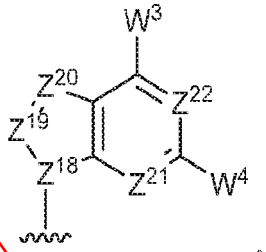

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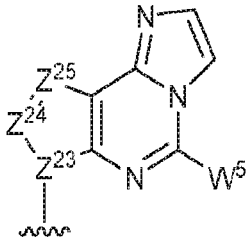

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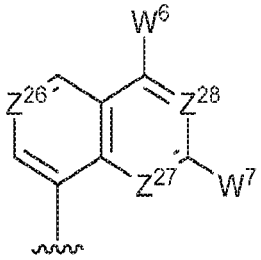

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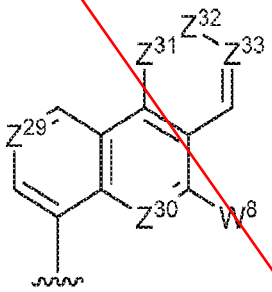

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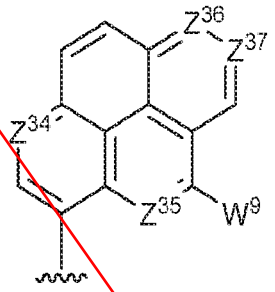
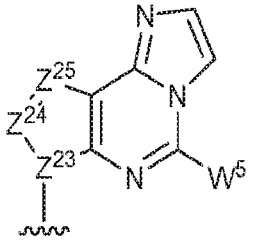
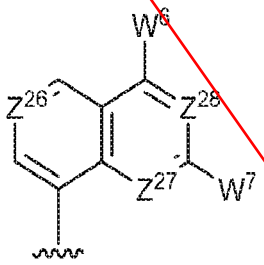
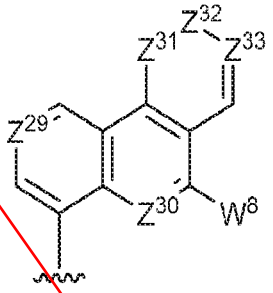
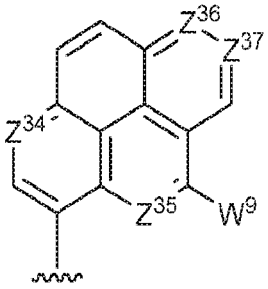



, with at least one of $R^{11}$ and $R^{12}$ being

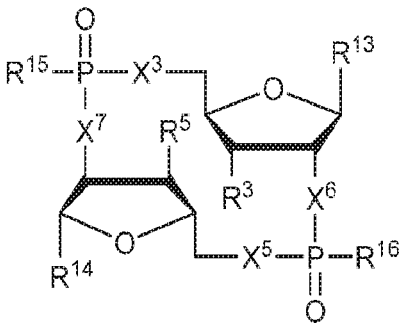




, , or ;

$Z^{12}$, $Z^{13}$, $Z^{14}$, $Z^{15}$, $Z^{16}$, $Z^{17}$, $Z^{18}$, $Z^{19}$, $Z^{20}$, $Z^{21}$, $Z^{22}$, $Z^{23}$, $Z^{24}$, $Z^{25}$, $Z^{26}$, $Z^{27}$, $Z^{28}$, $Z^{29}$, $Z^{30}$, $Z^{31}$, $Z^{32}$, $Z^{33}$, $Z^{34}$, $Z^{35}$, $Z^{36}$, and $Z^{37}$ are each independently CH or N; and

$W^3$, $W^4$, $W^5$, $W^6$, $W^7$, $W^8$, and $W^9$ are independently hydrogen, halogen, hydroxyl, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, di($C_{1\text{-}6}$alkyl)amino, or azido groups, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, di($C_{1\text{-}6}$alkyl)amino, or azido groups, $C_{3\text{-}5}$alkenyl-O-, $C_{3\text{-}5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or $-NR^7R^8$.

9. The compound of claim 1, wherein a compound of Formula **Ii**, or a pharmaceutically acceptable salt thereof,

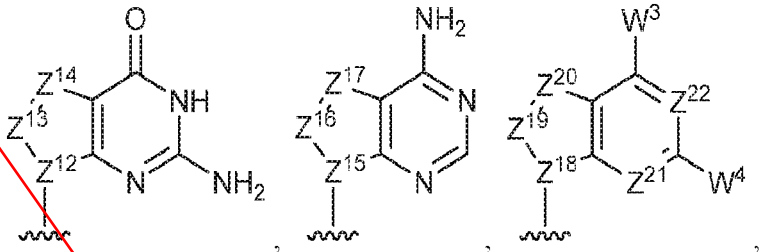


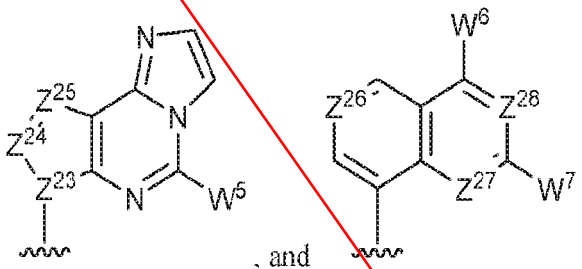
Formula **Ii**

wherein:

$X^3$, $X^5$, $X^6$, and $X^7$ are independently O, NH, $CH_2$, CHF, or $CF_2$;

$R^{13}$ and $R^{14}$ are independently selected from the group consisting of:




, and ,

$Z^{12}$, $Z^{13}$, $Z^{14}$, $Z^{15}$, $Z^{16}$, $Z^{17}$, $Z^{18}$, $Z^{19}$, $Z^{20}$, $Z^{21}$, $Z^{22}$, $Z^{23}$, $Z^{24}$, $Z^{25}$, $Z^{26}$, $Z^{27}$, and $Z^{28}$ are each independently CH or N; and

$W^3$, $W^4$, $W^5$, $W^6$, and $W^7$ are independently hydrogen, halogen, hydroxyl, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, di($C_{1\text{-}6}$alkyl)amino, or azido groups, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, di($C_{1\text{-}6}$alkyl)amino, or azido groups, $C_{3\text{-}5}$alkenyl-O-, $C_{3\text{-}5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or $-NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, di($C_{1\text{-}6}$alkyl)amino, or azido groups, cyclic -($C_{1\text{-}6}$alkyl)-, cyclic -($C_{1\text{-}6}$alkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, or di($C_{1\text{-}6}$alkyl)amino groups, cyclic -($C_{1\text{-}6}$oxaalkyl)-, or cyclic -($C_{1\text{-}6}$oxaalkyl)- selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, or di($C_{1\text{-}6}$alkyl)amino groups;

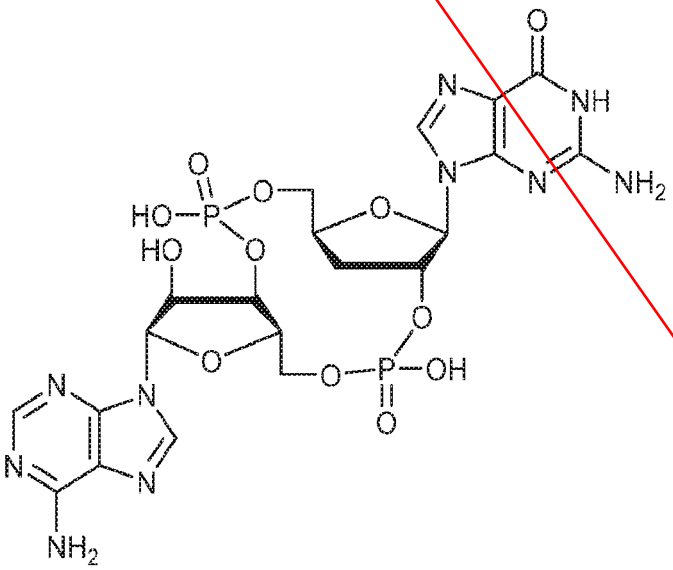
$R^3$ and $R^5$ are independently hydrogen, halogen, hydroxyl, amino, $C_{1-6}$alkyl, $C_{1-6}$alkyl selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{1-6}$alkoxy, $C_{1-6}$alkoxy selectively functionalized with one or more halogen, thiol, hydroxyl, carbonyl, carboxyl, carbonyloxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups, $C_{3-5}$alkenyl-O-, $C_{3-5}$alkynyl-O-, oligo(ethylene glycol), poly(ethylene glycol), azido, or $-NR^7R^8$;

$R^{15}$ and $R^{16}$ are independently hydroxyl, thiol, methoxy, ethoxy, amino, *N*-methylamino, *N,N*-dimethylamino, *N*-ethylamino, *N,N*-diethylamino, *N*-morpholino, or borano ($-BH_3^-$);

the oxygen atom in one or both of the tetrahydrofuranyl rings of Formula **Ii** can be optionally replaced by a sulfur or a selenium atom; and

the compound is not 2'2'-cGAMP.

10. A compound selected from the group consisting of:



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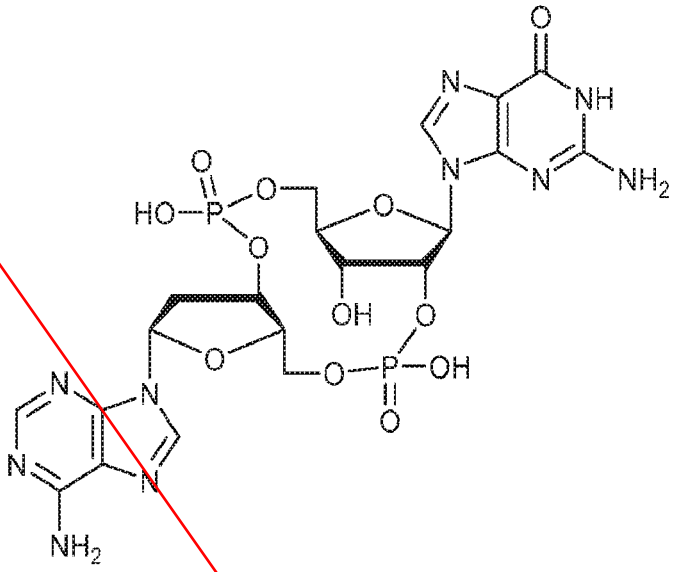

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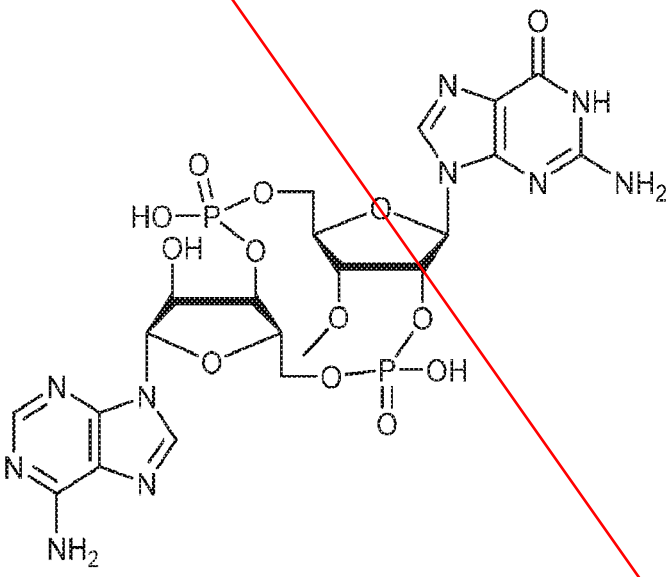

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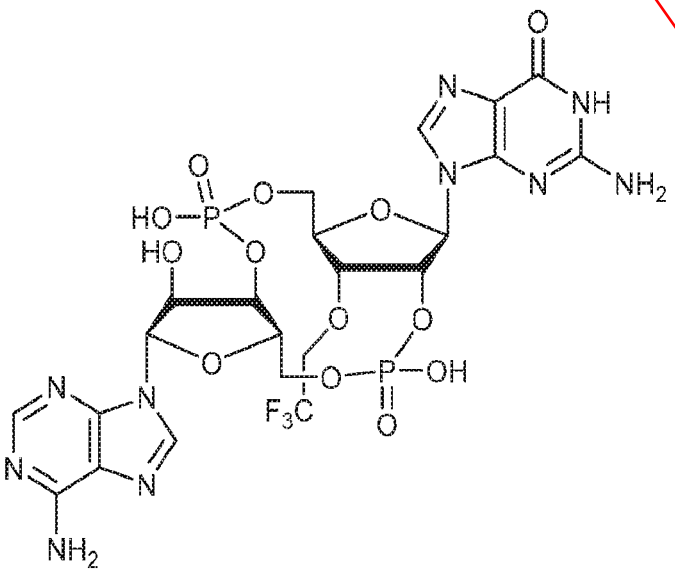

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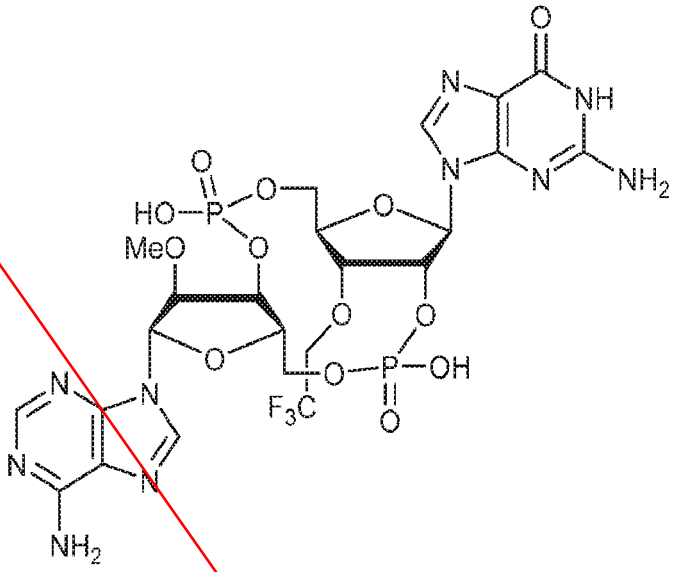

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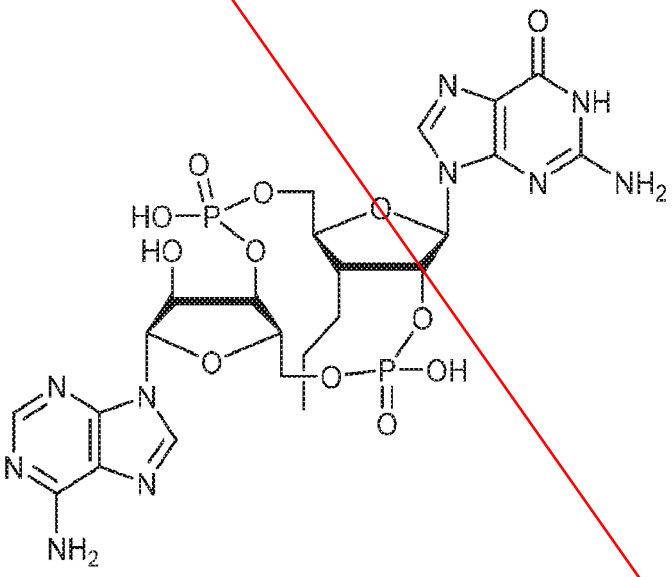

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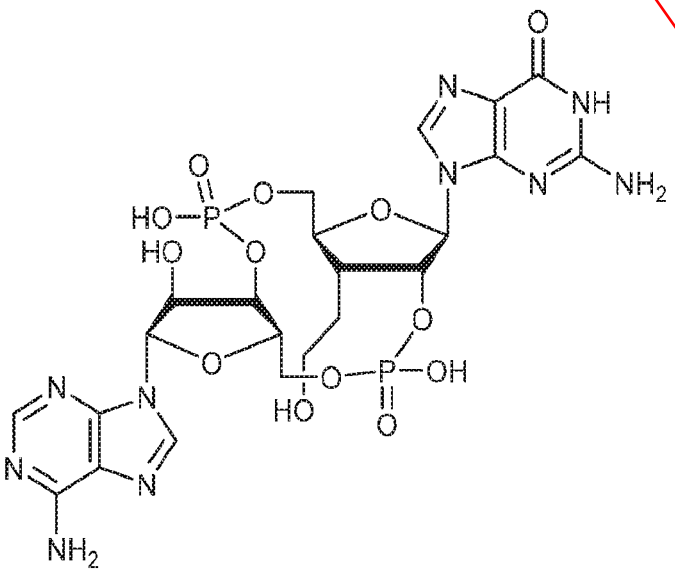

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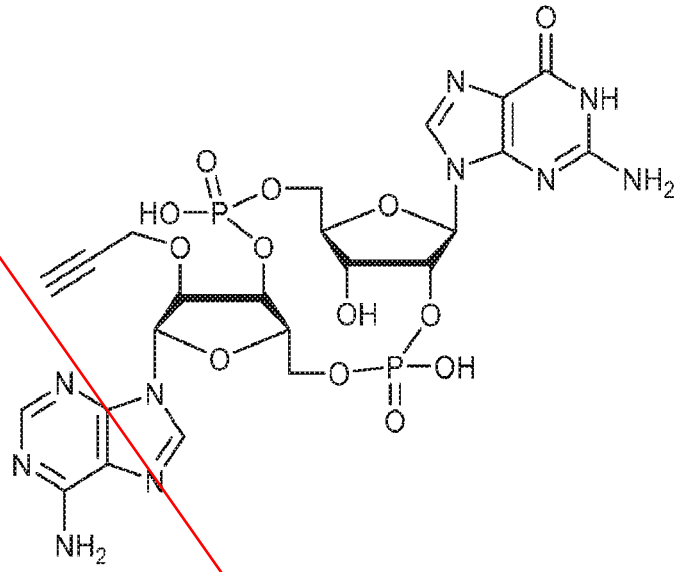

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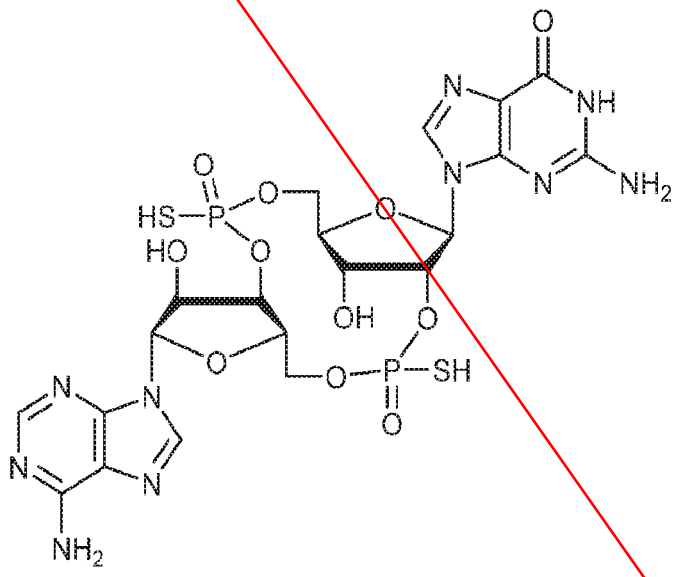

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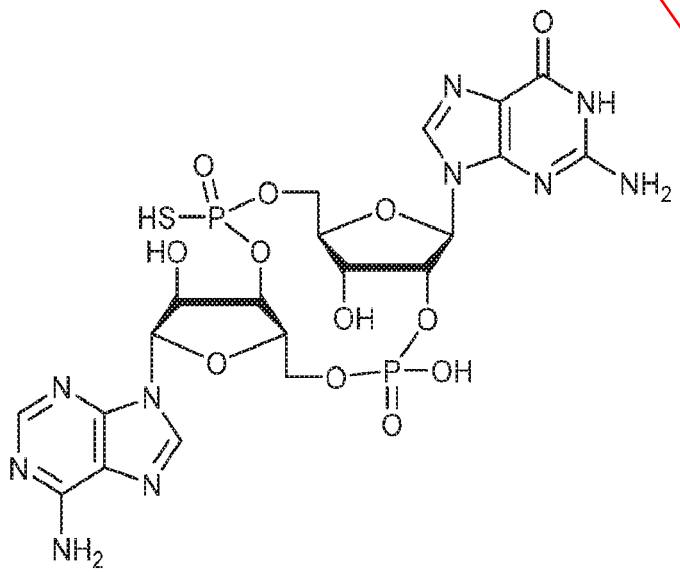

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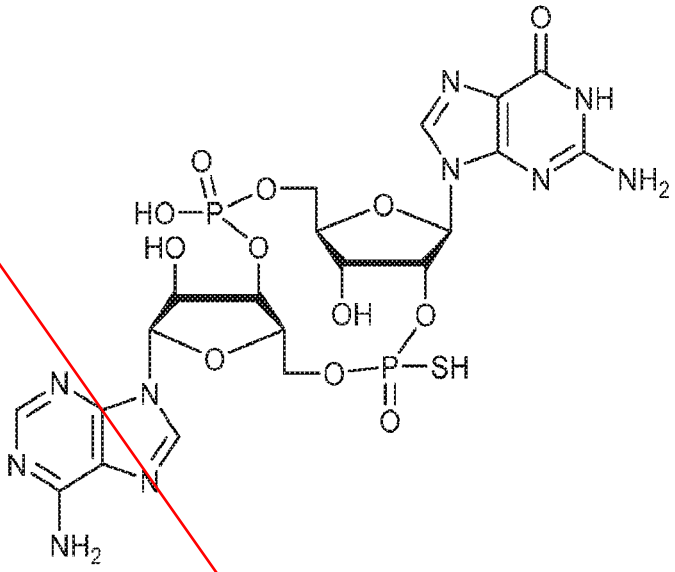

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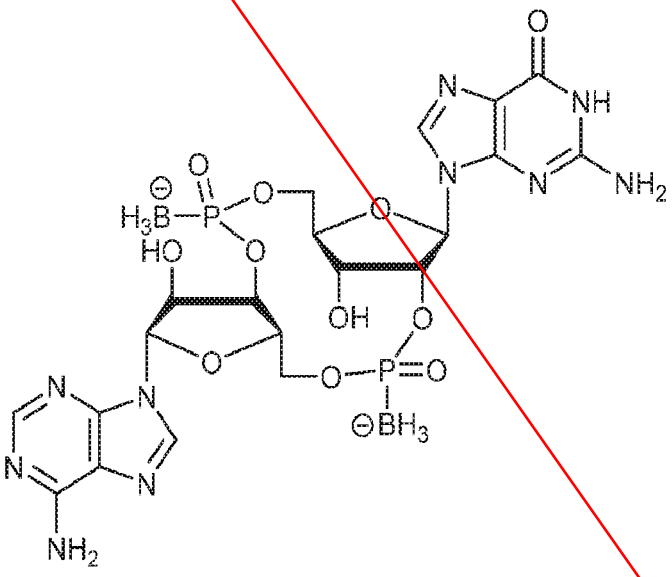

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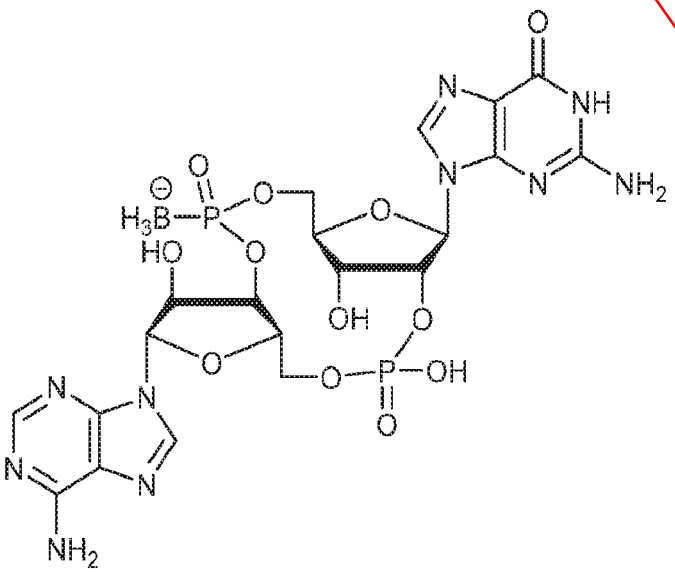

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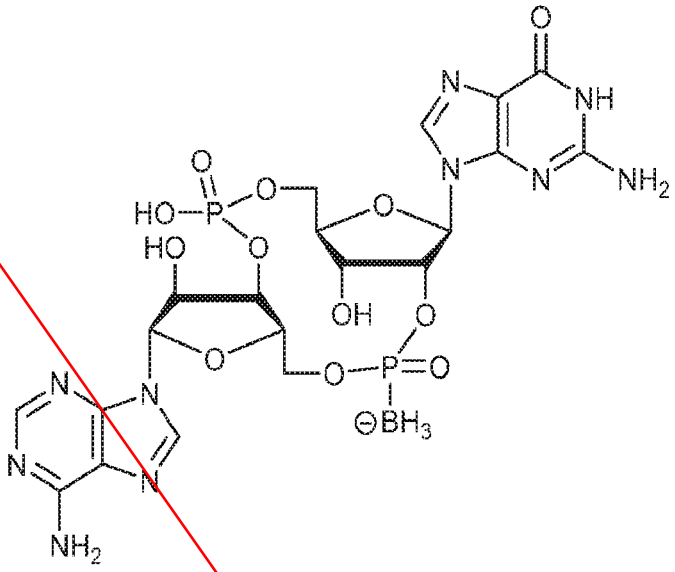

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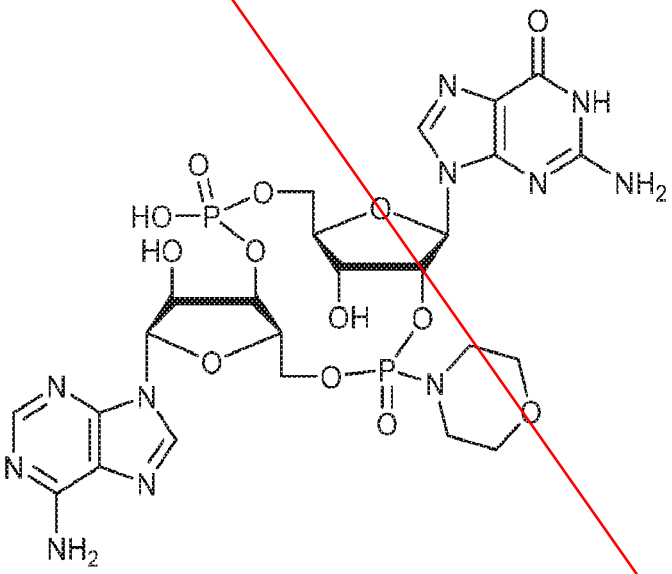

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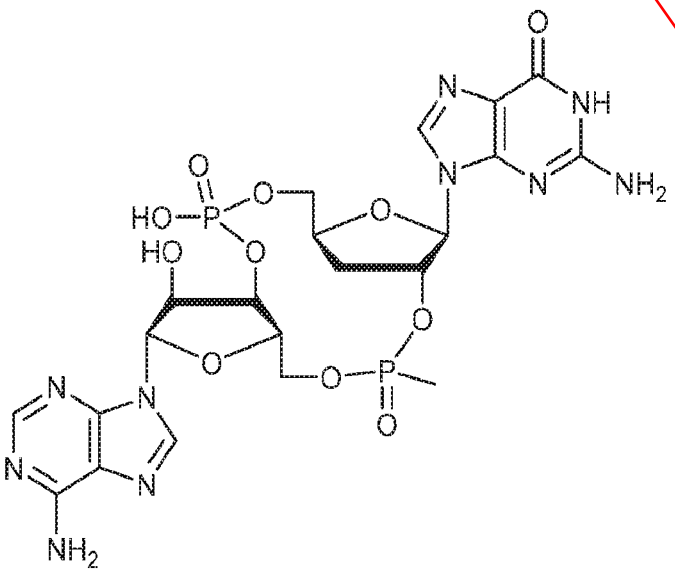

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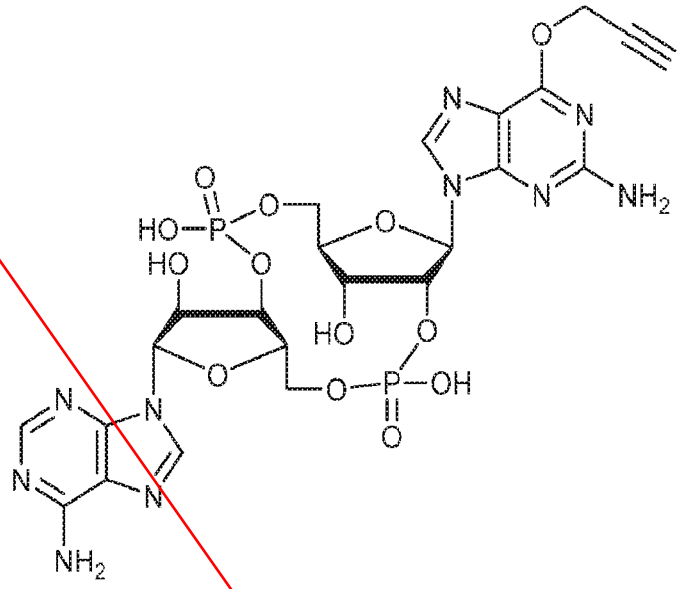

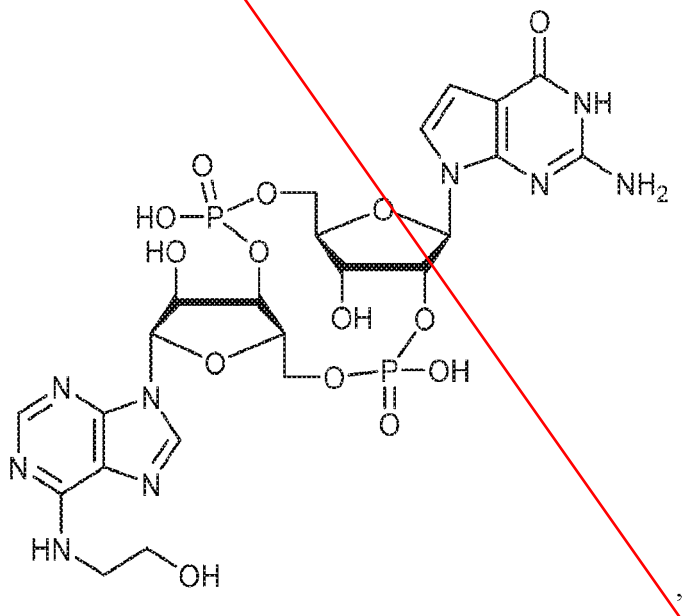

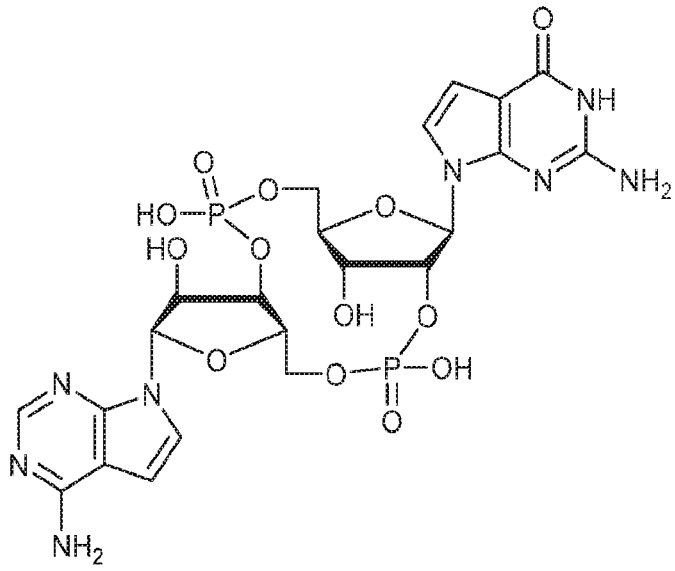

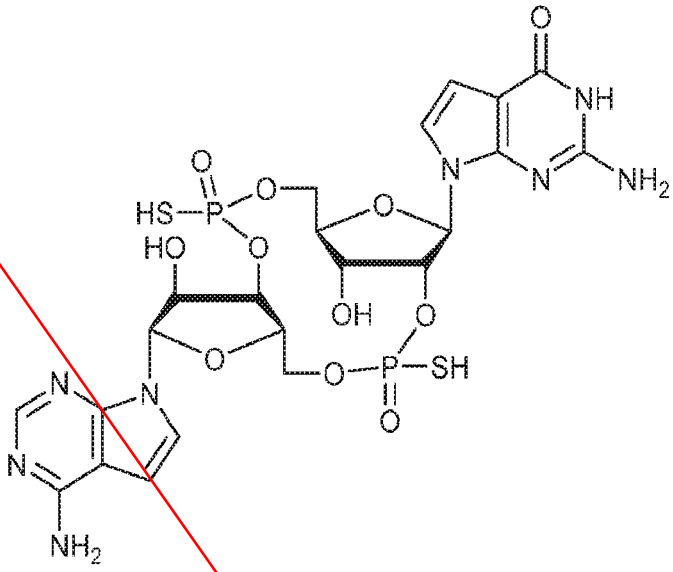

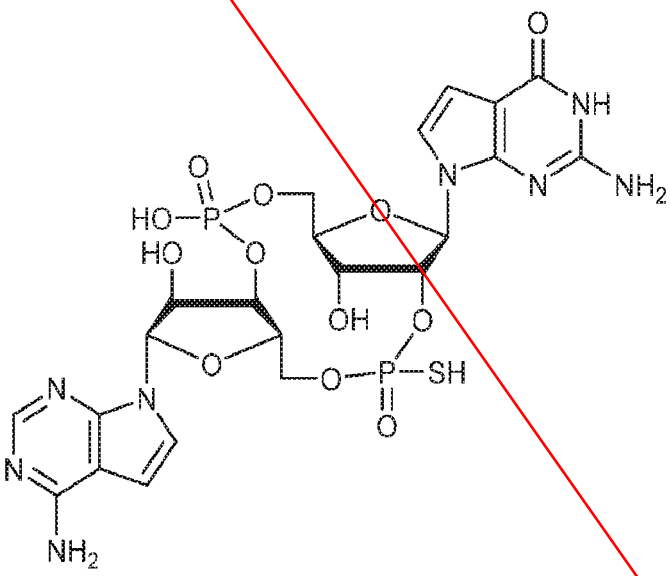

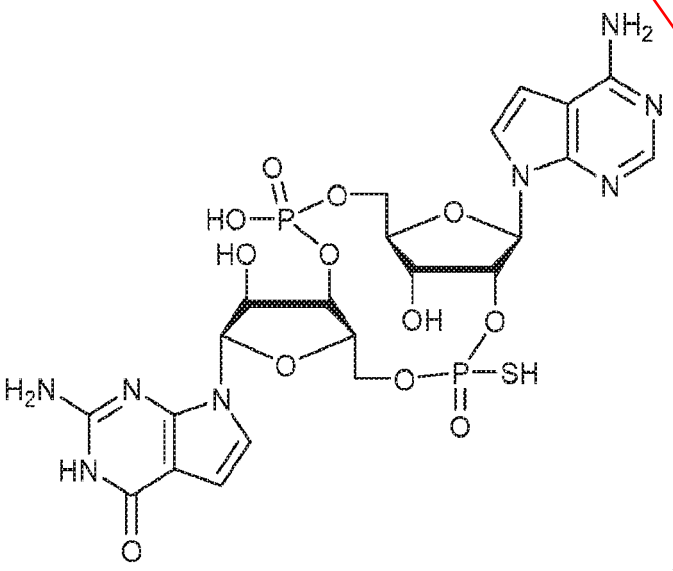

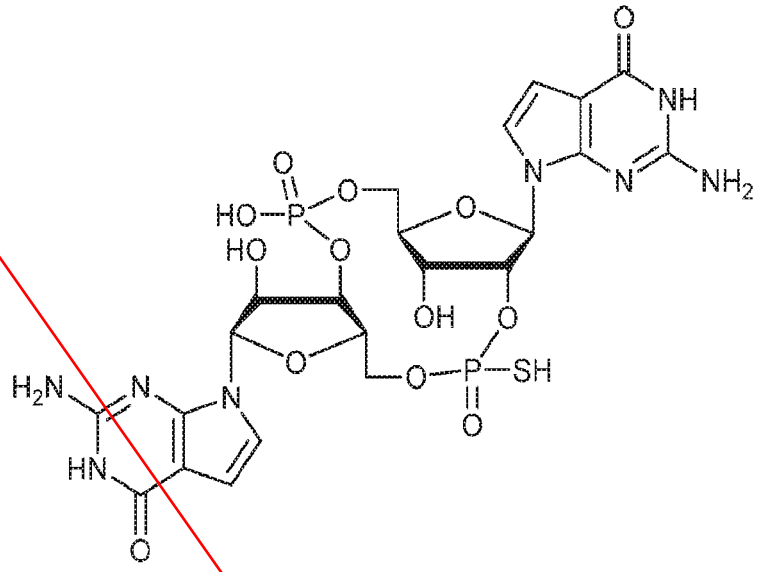

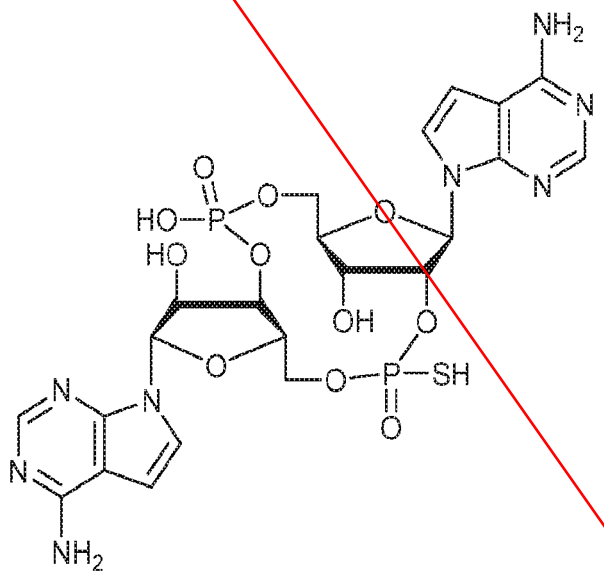

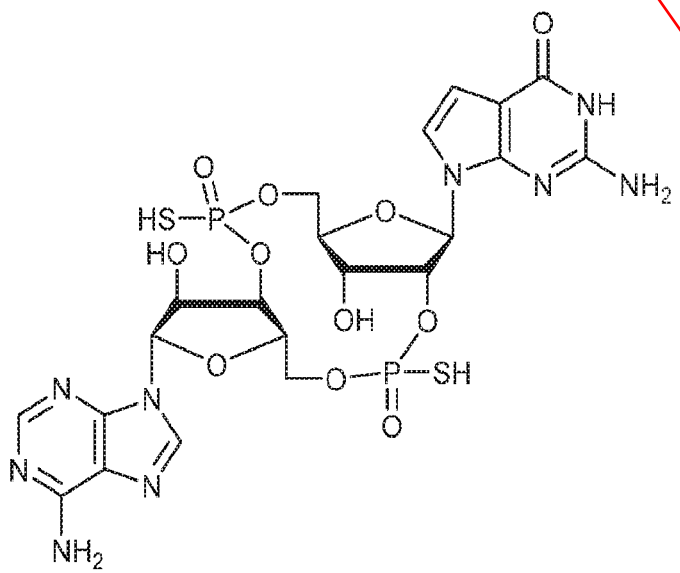

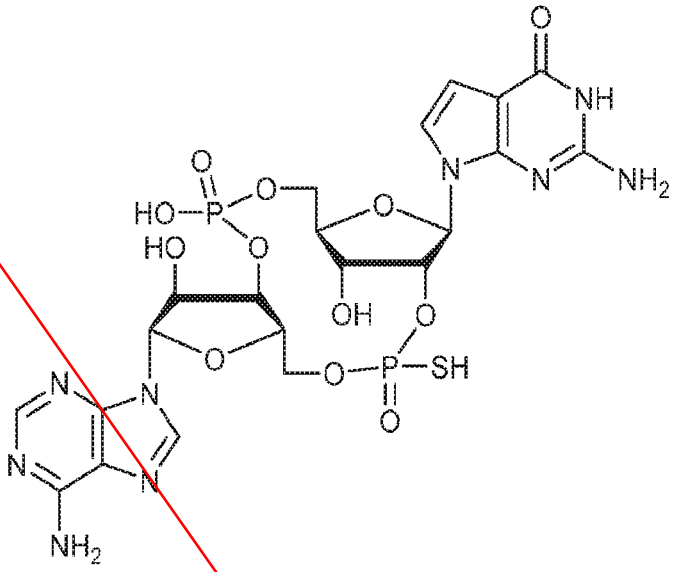

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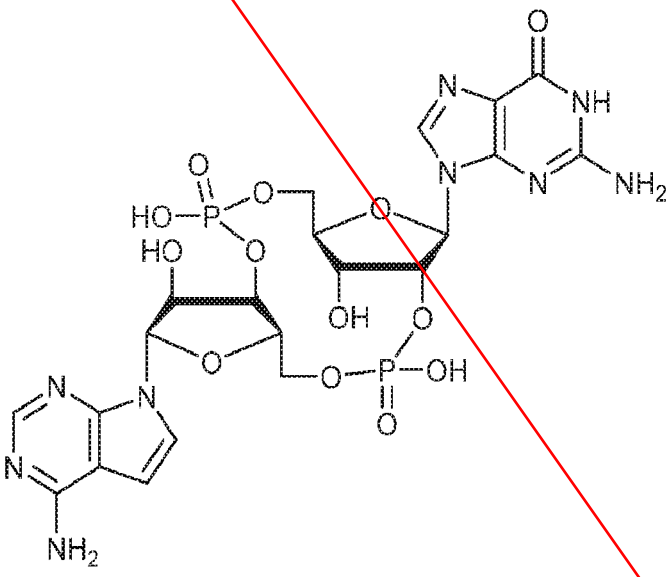

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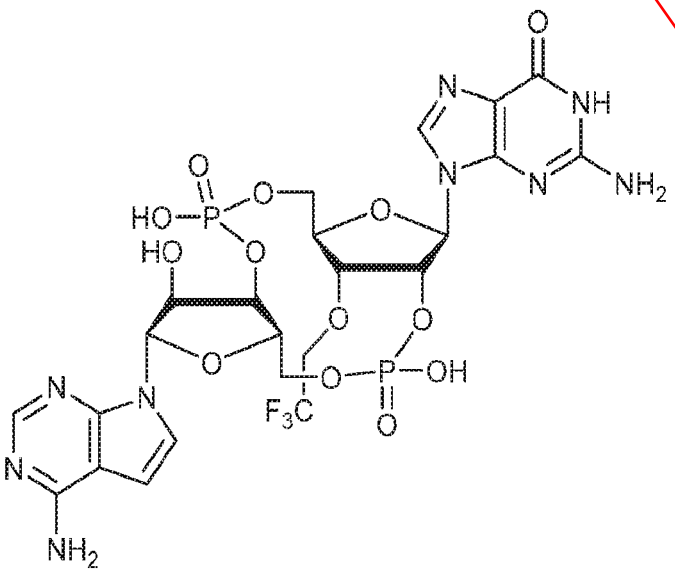

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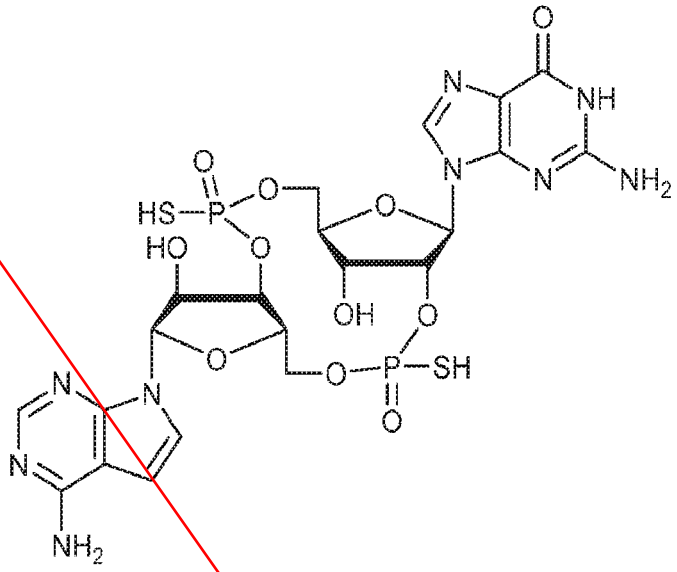

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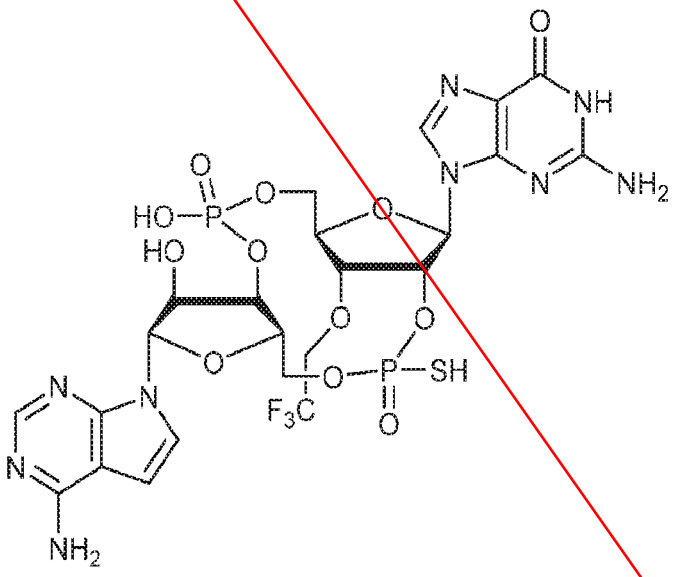

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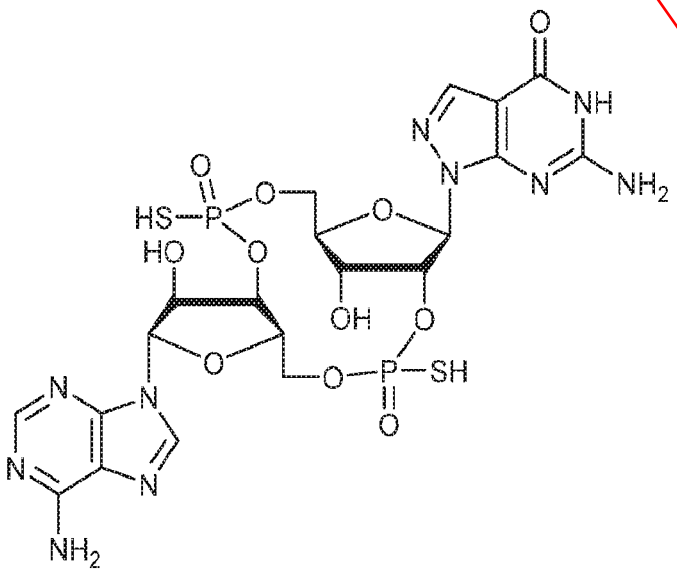

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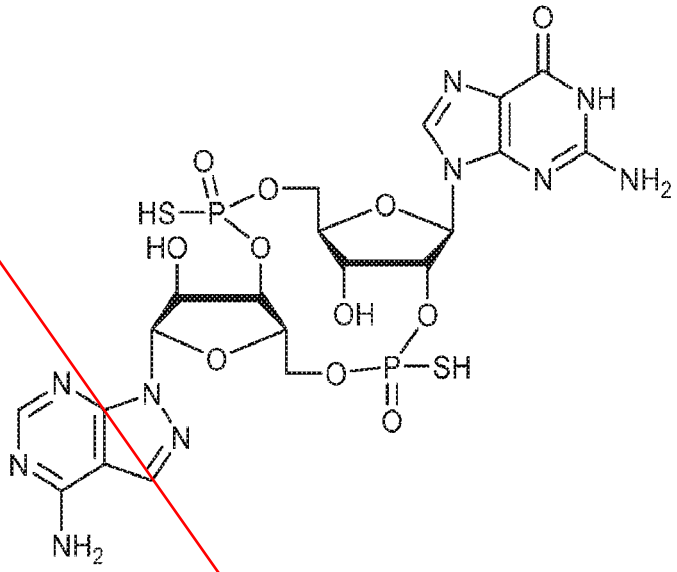

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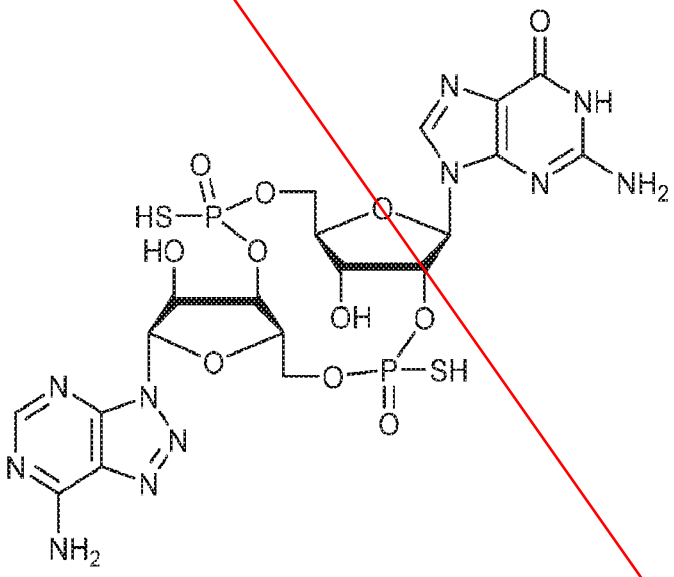

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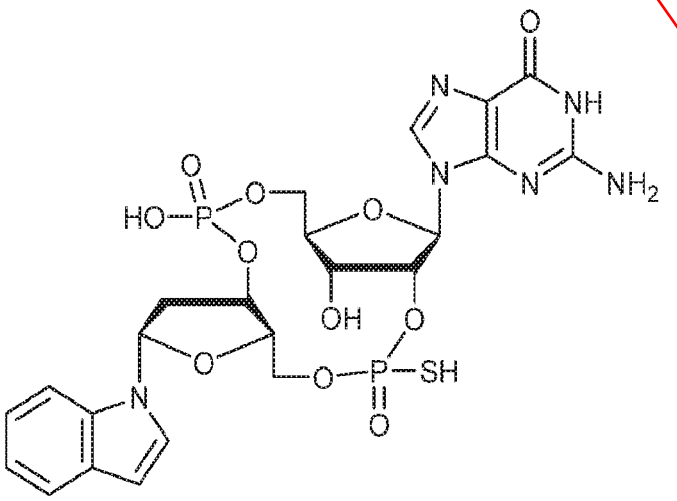

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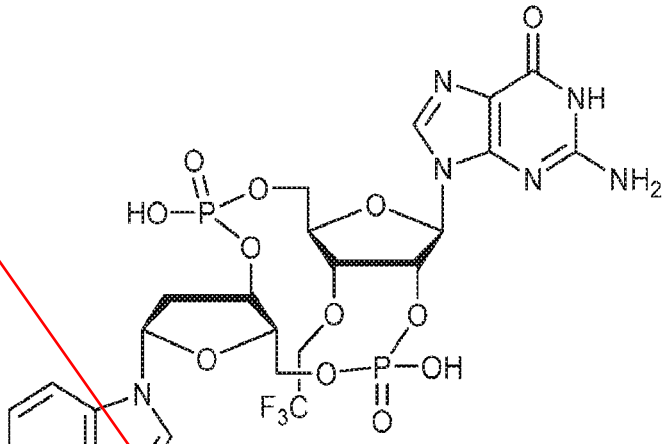

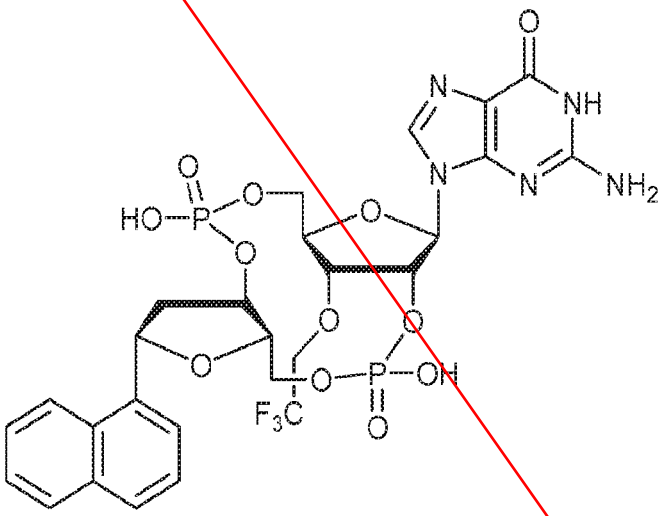

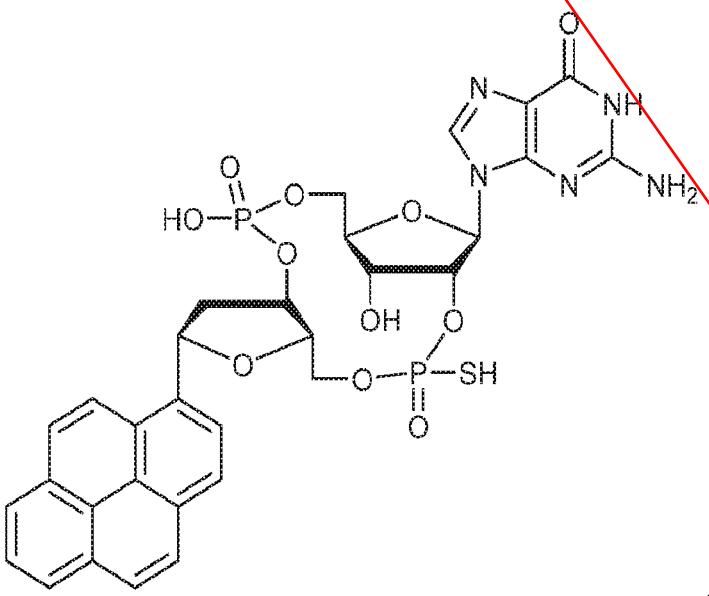

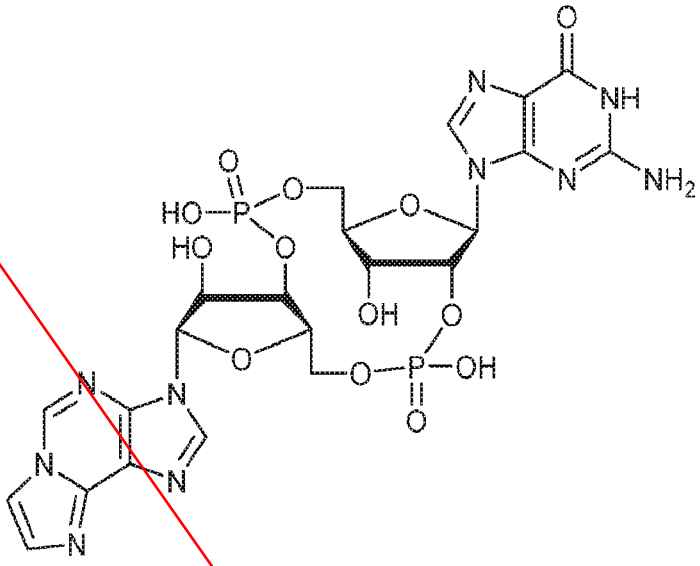

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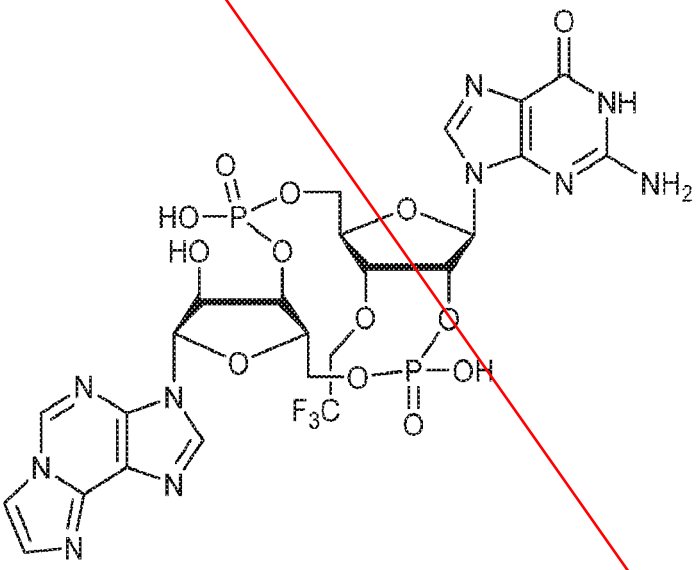

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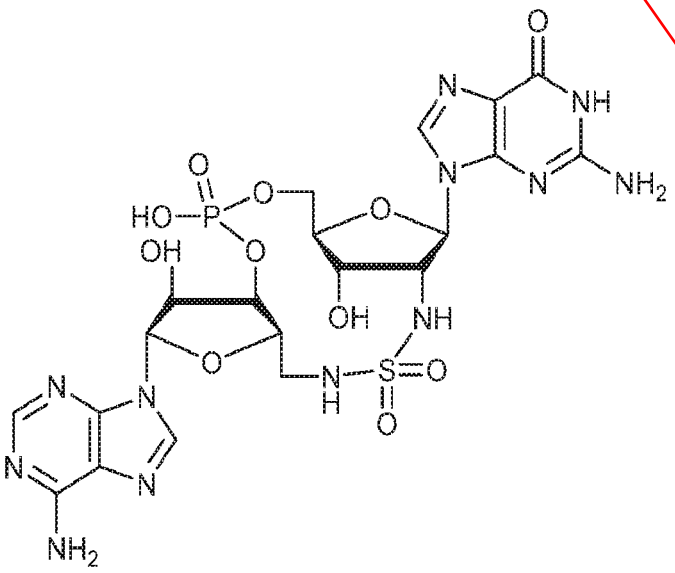

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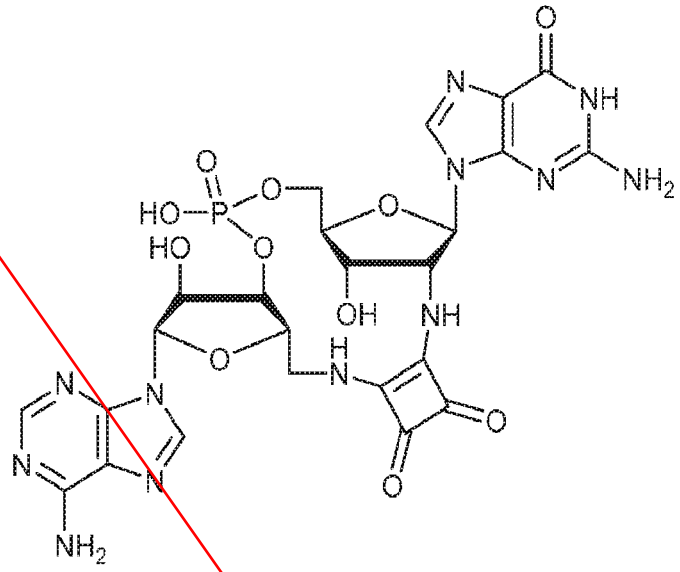
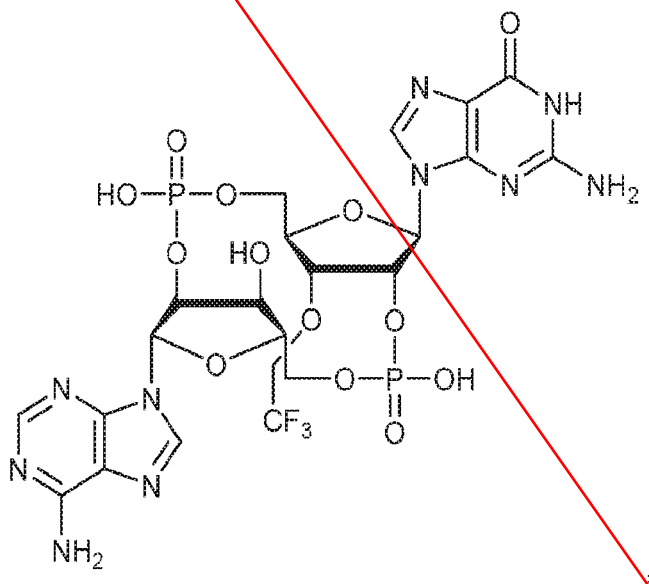
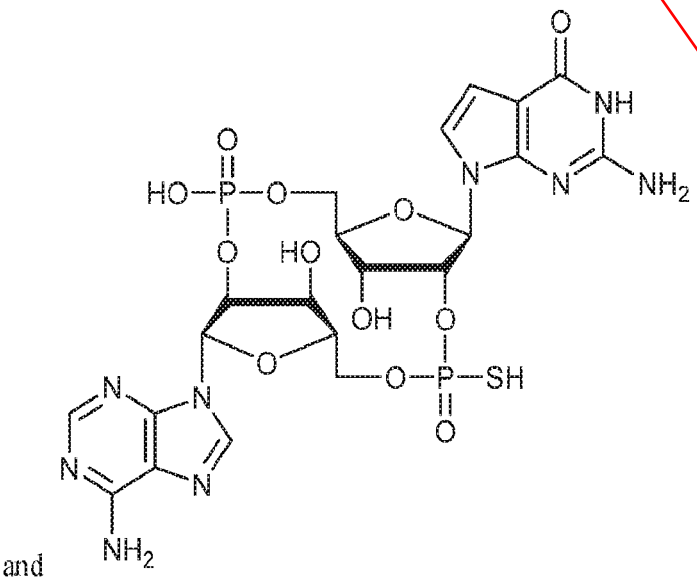
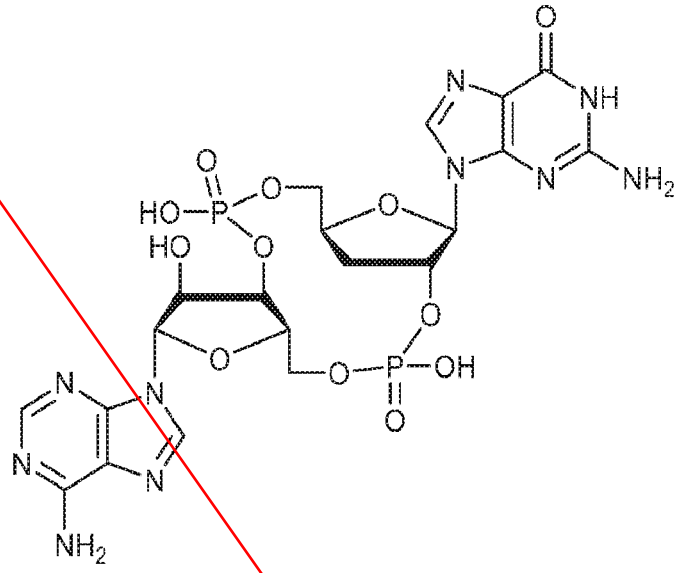






and

11. A compound selected from the group consisting of:



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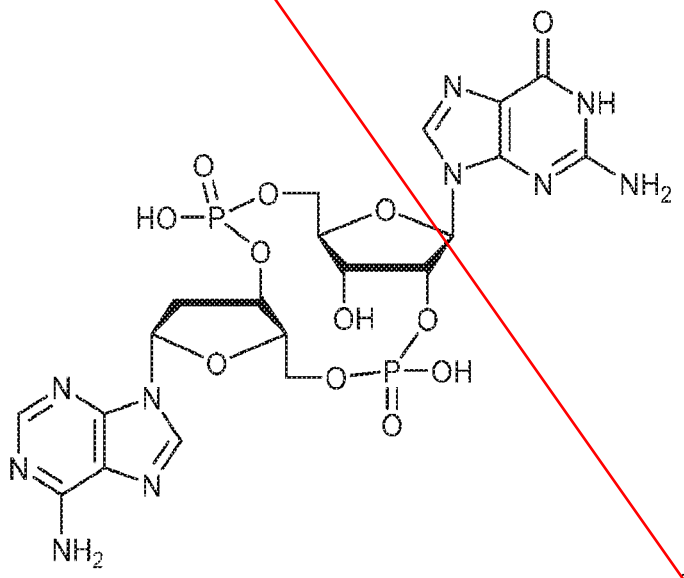

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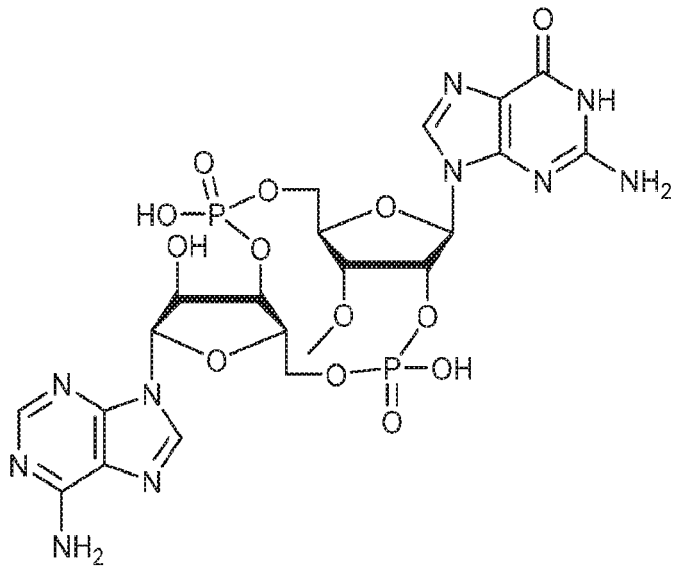

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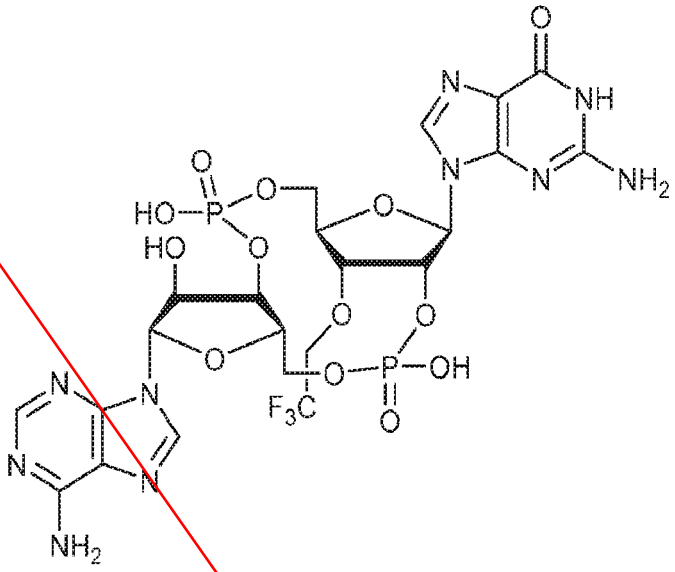

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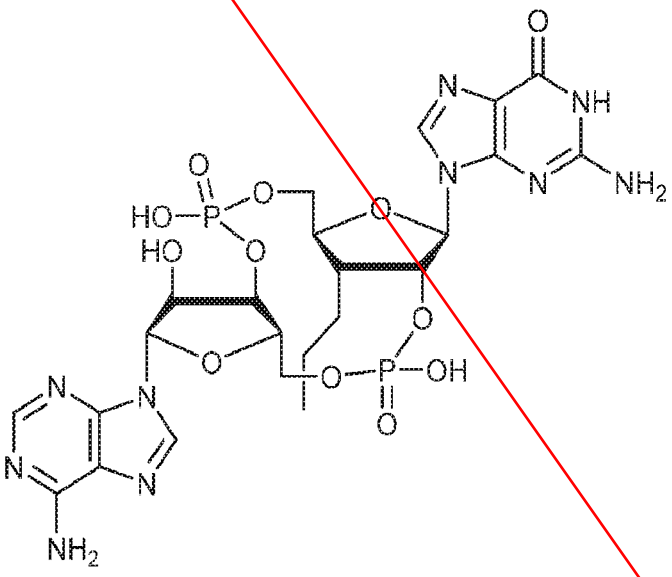

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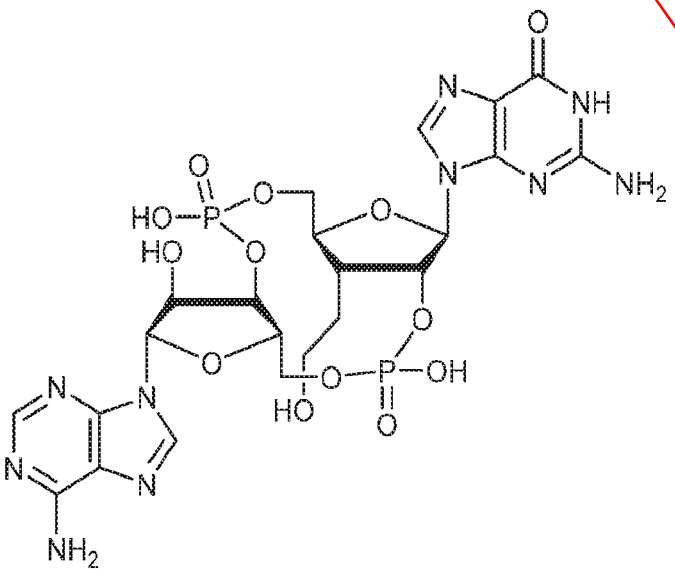

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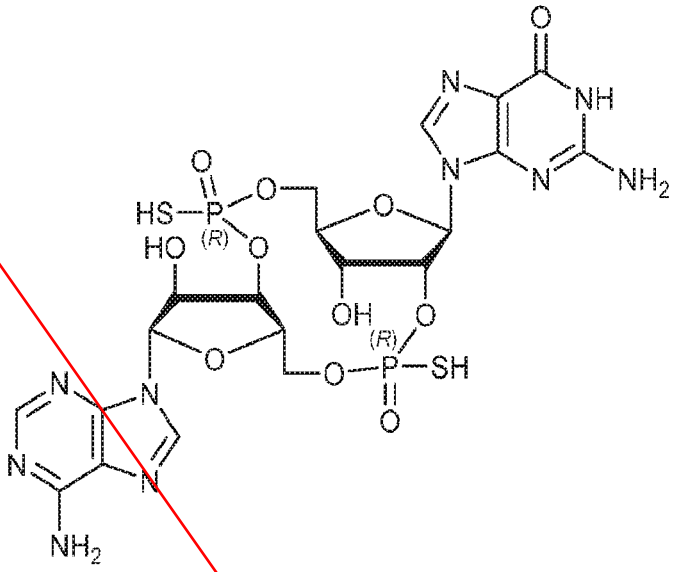

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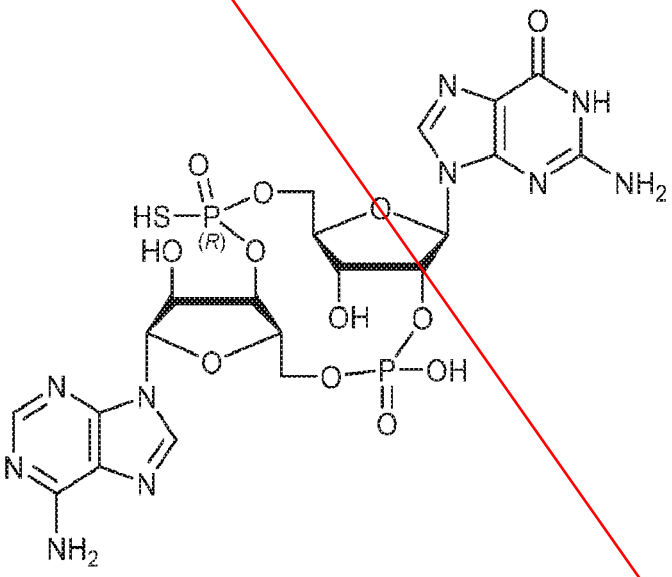

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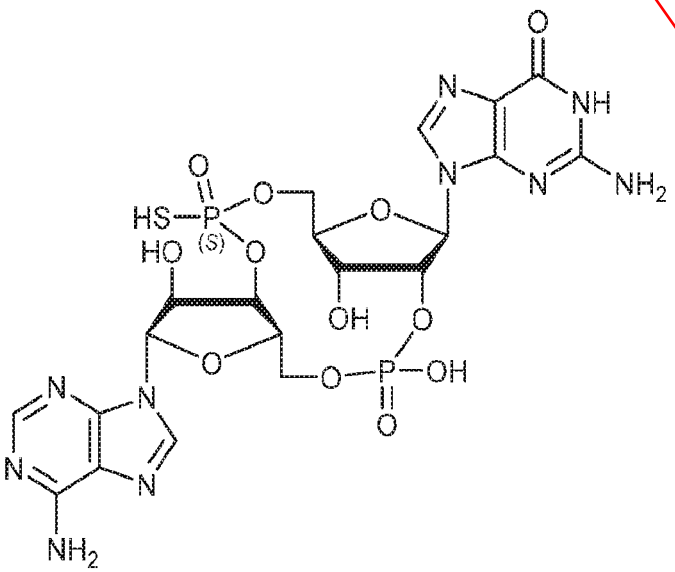

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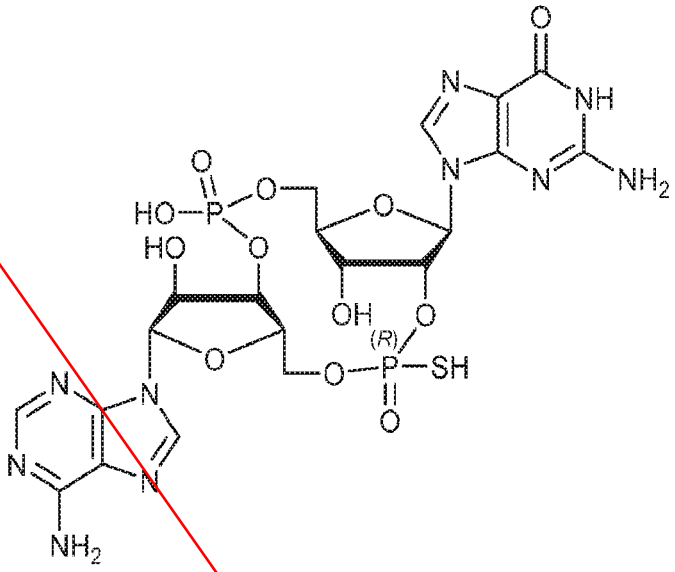

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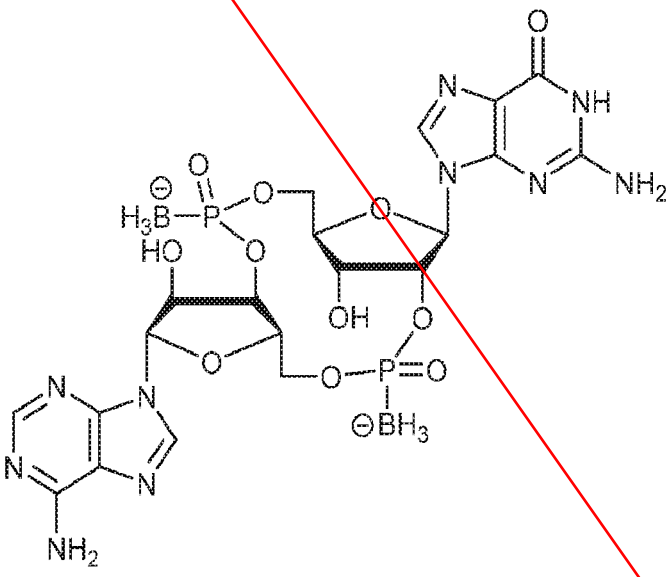

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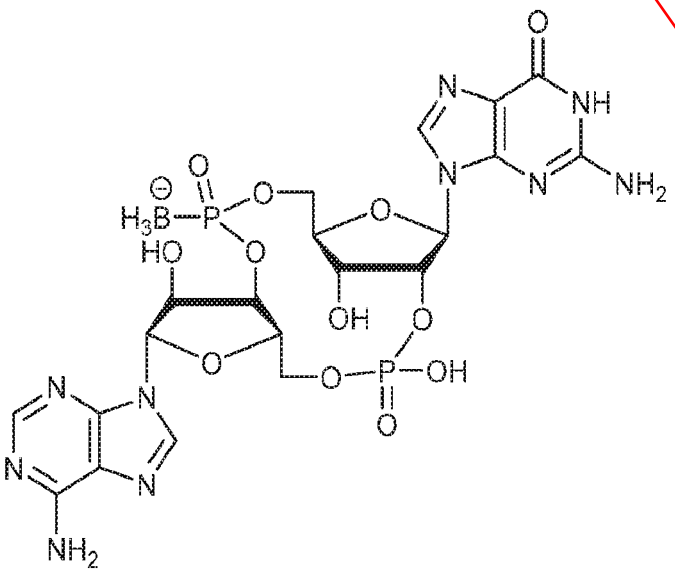

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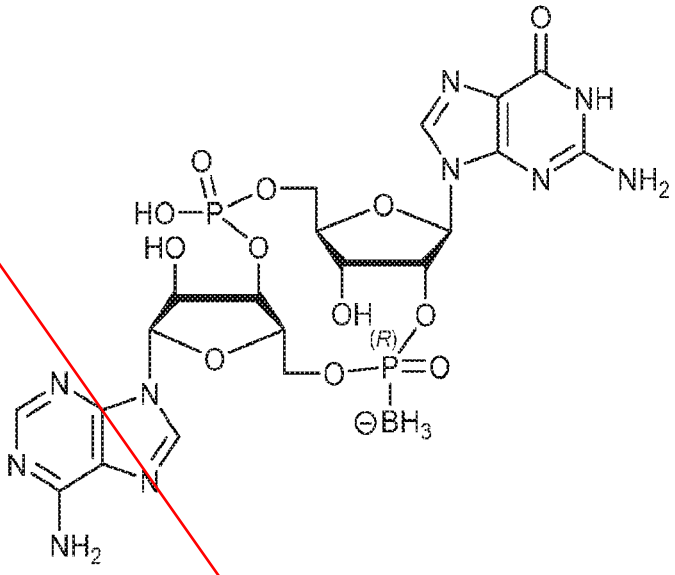

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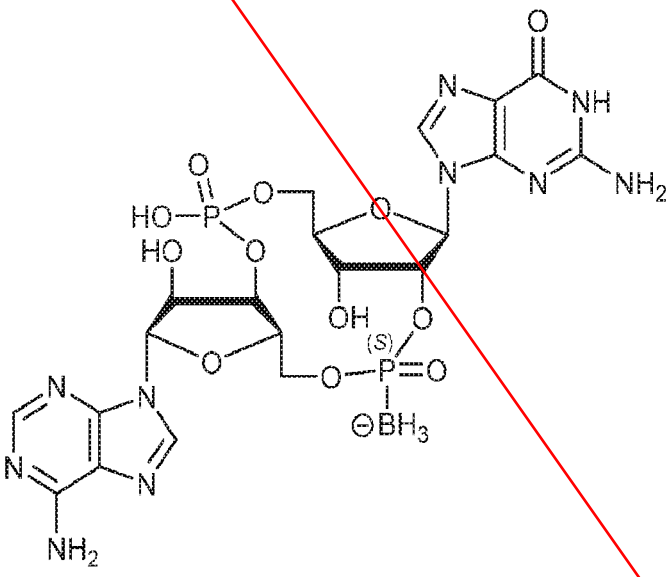

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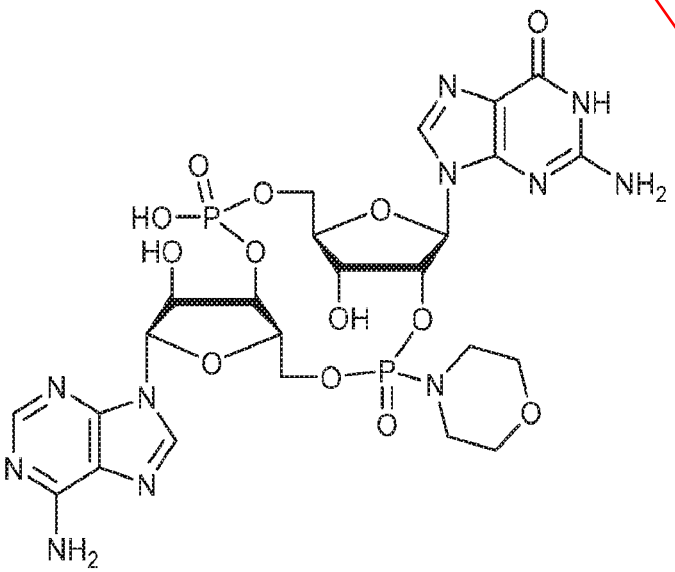

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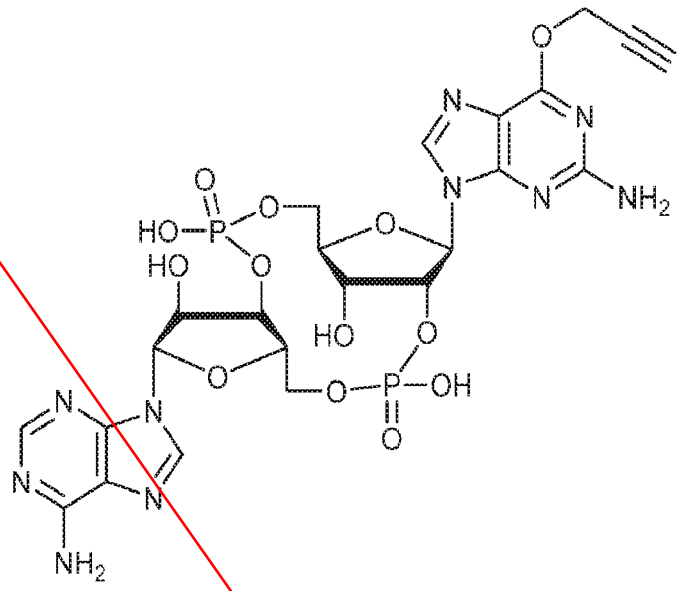

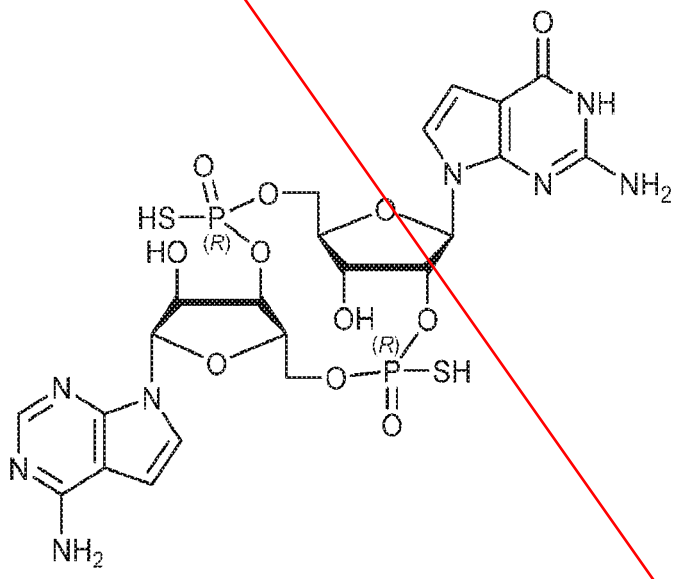

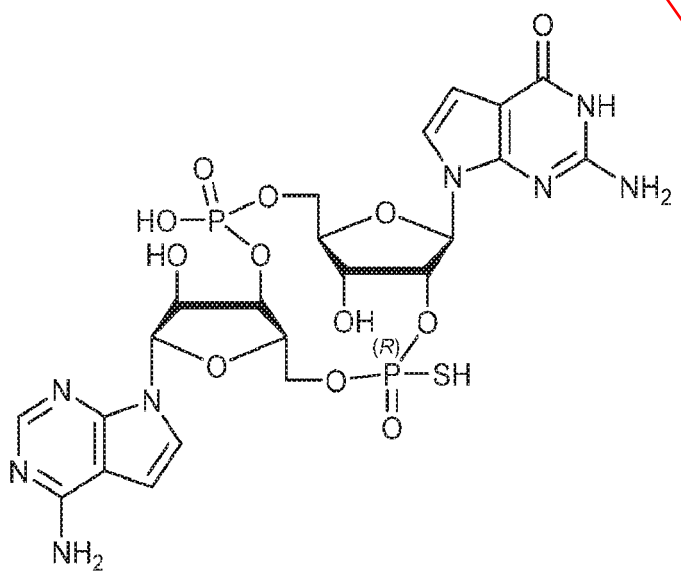

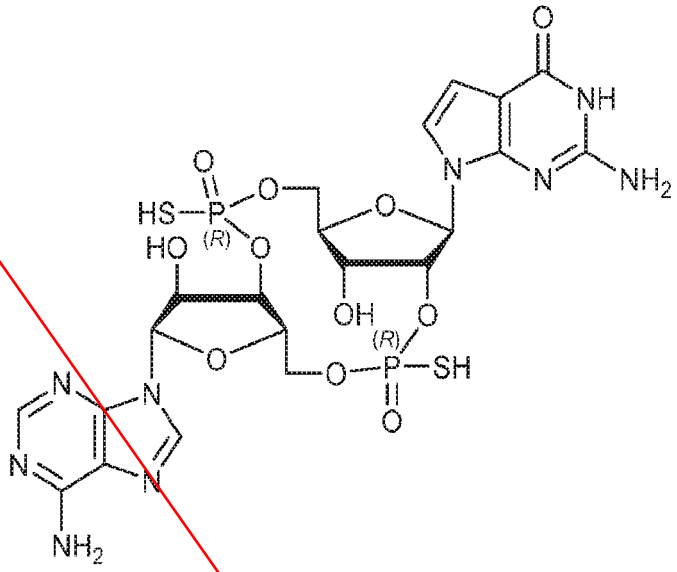

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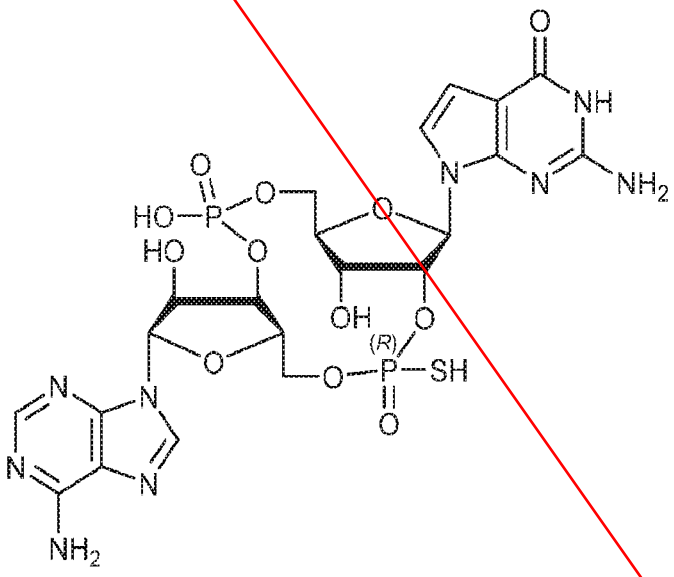

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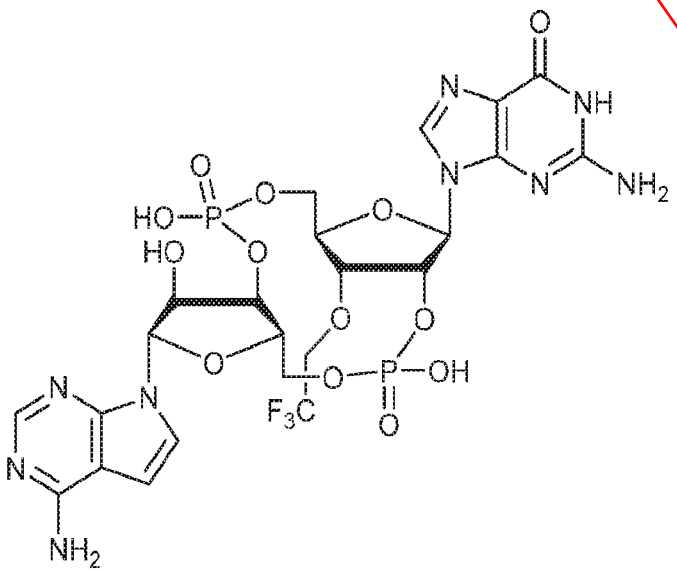

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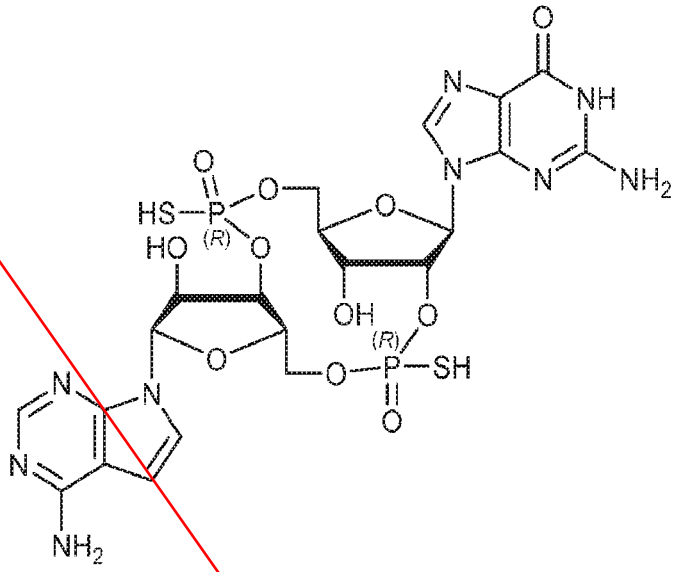

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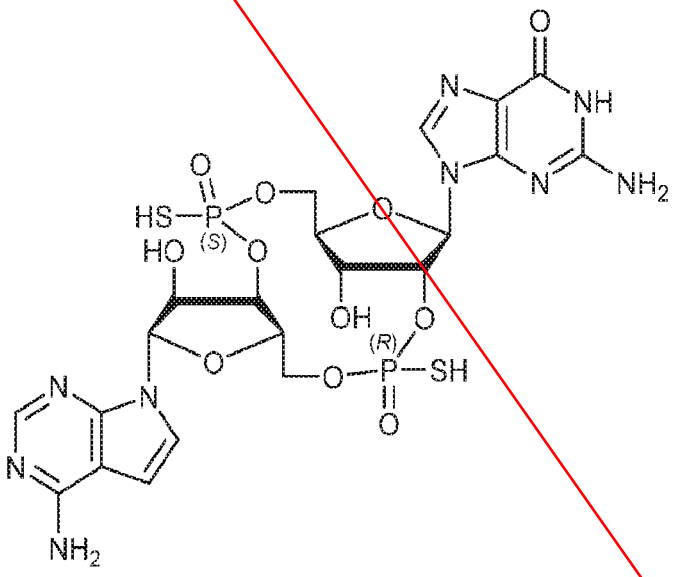

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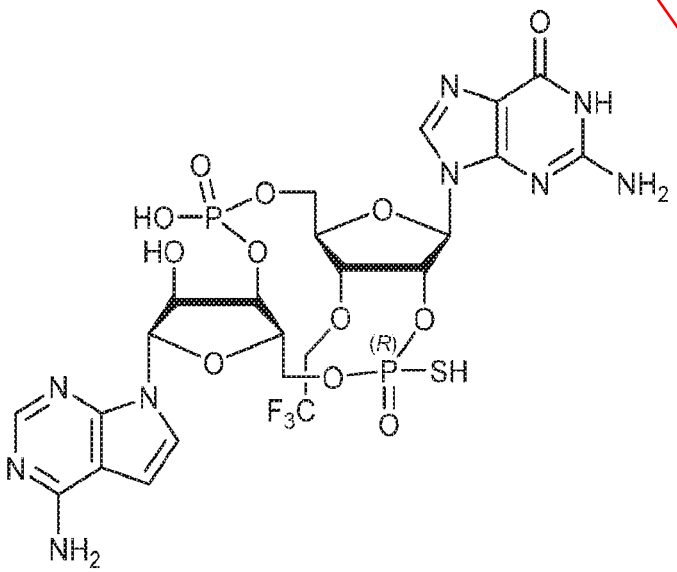

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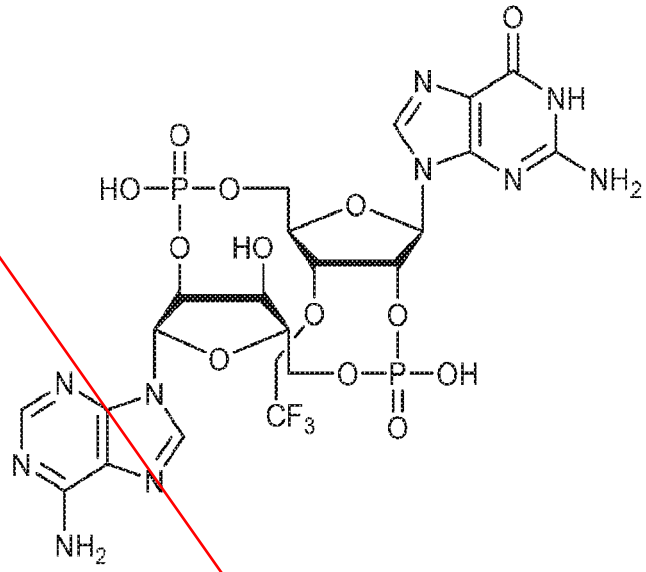

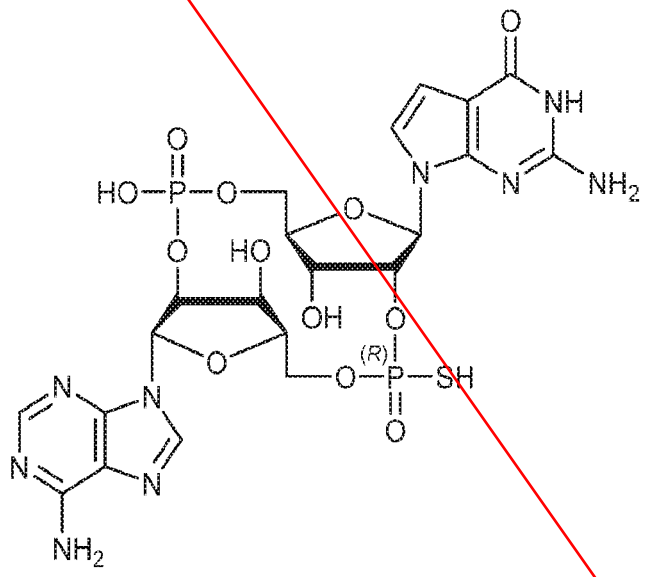

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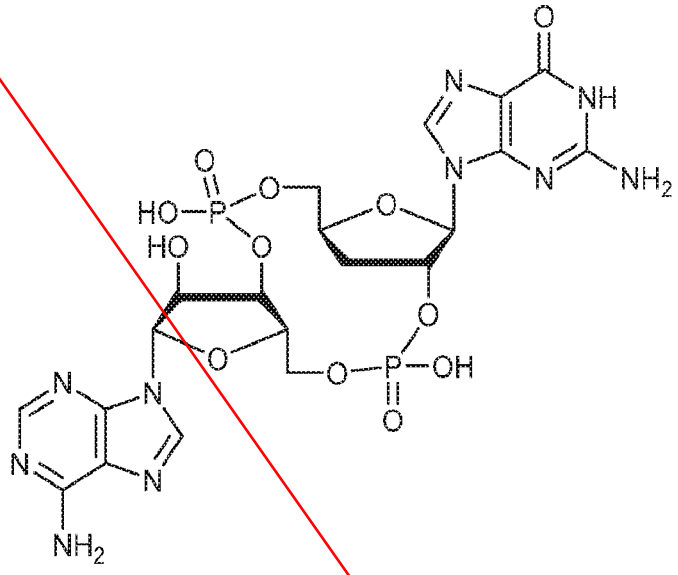
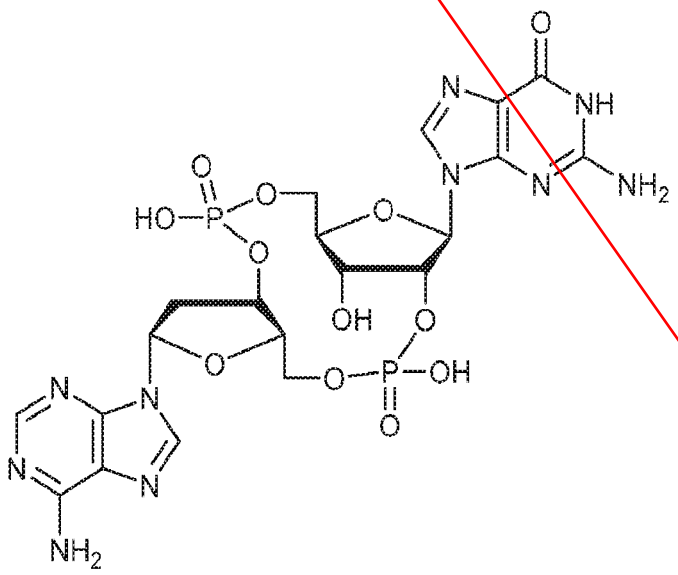
12. A compound according to the formula:



13. A compound according to the formula:



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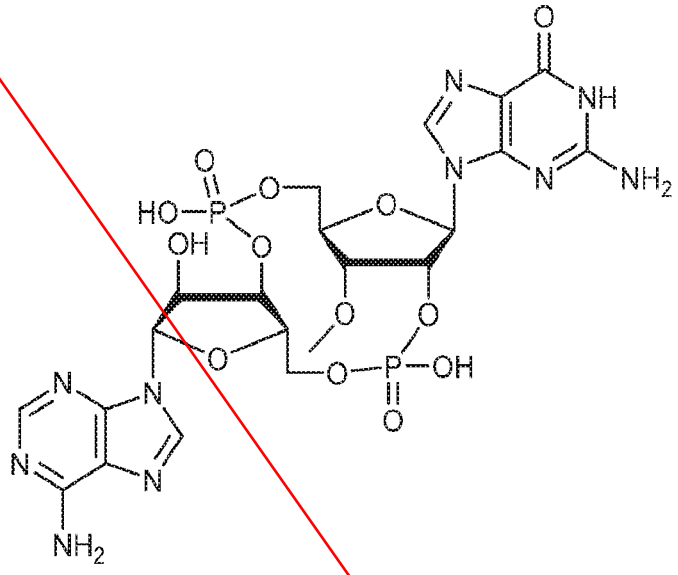
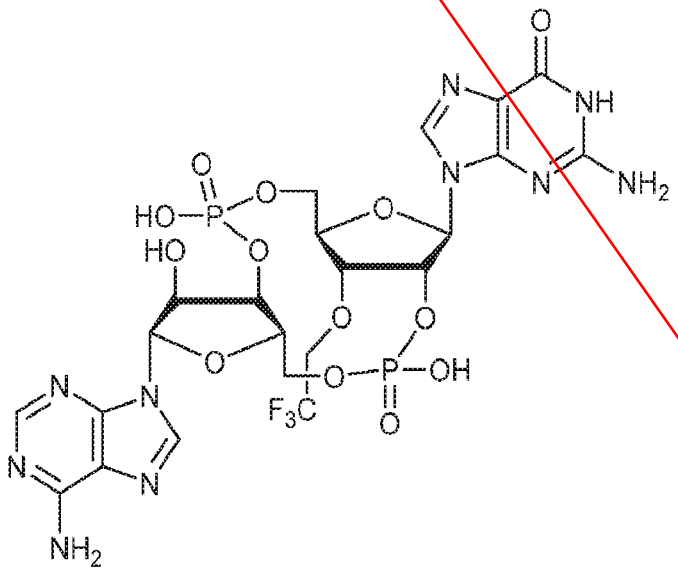
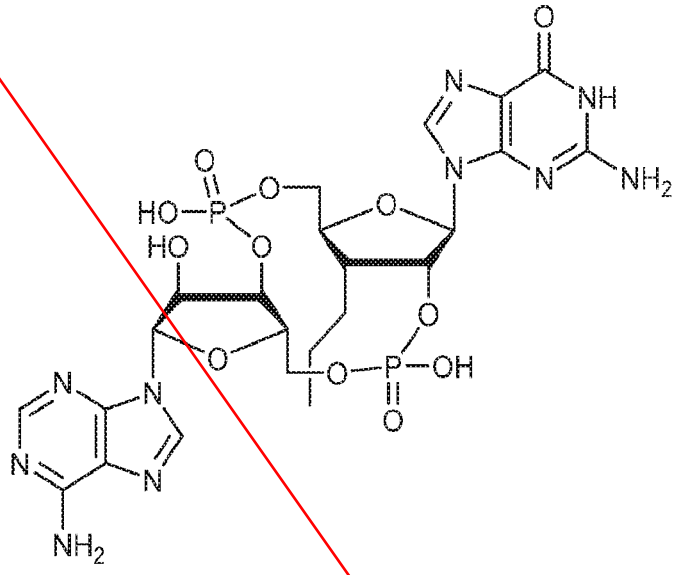


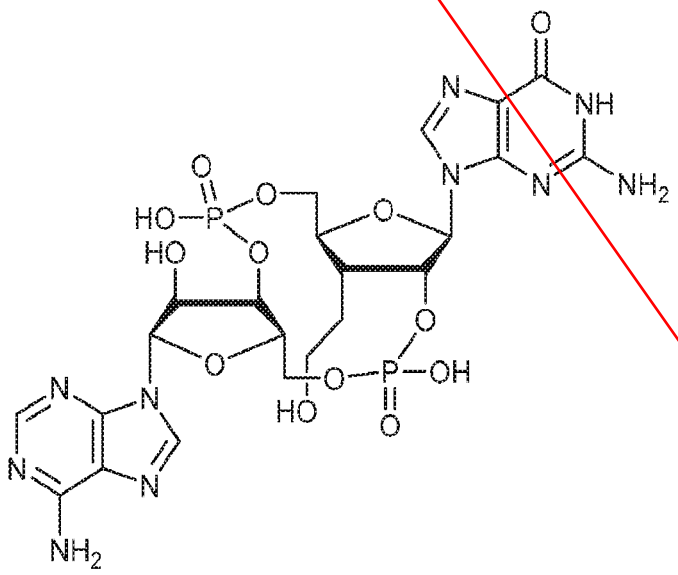
15. A compound according to the formula:



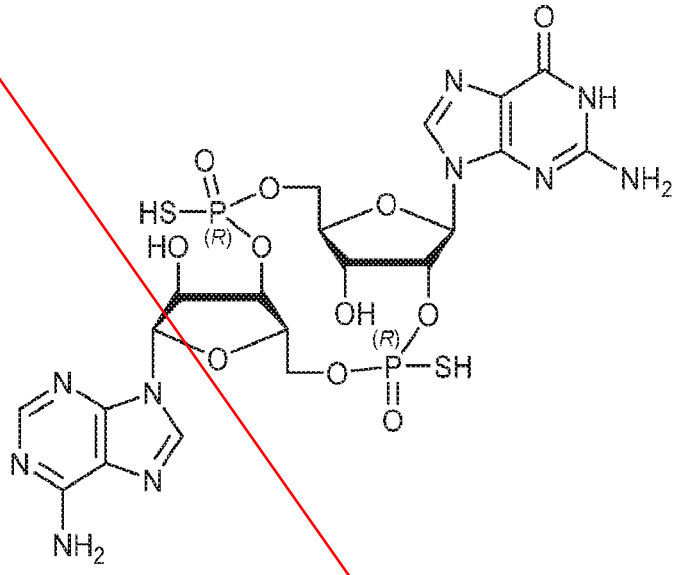
16. A compound according to the formula:



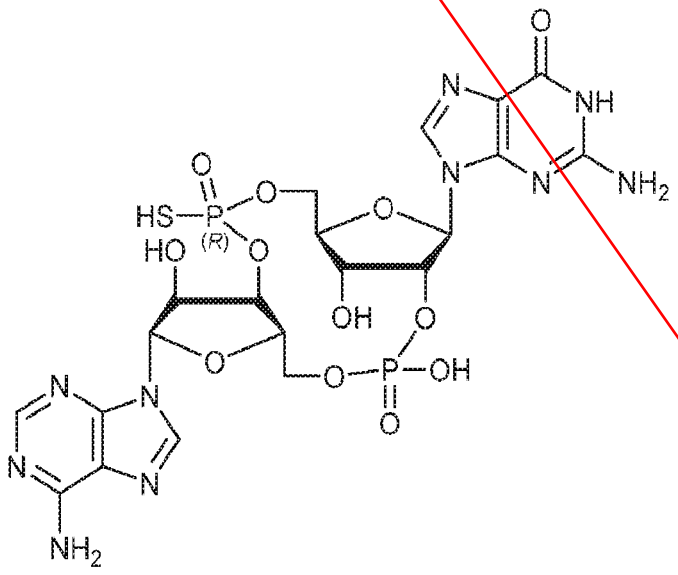
17. A compound according to the formula:



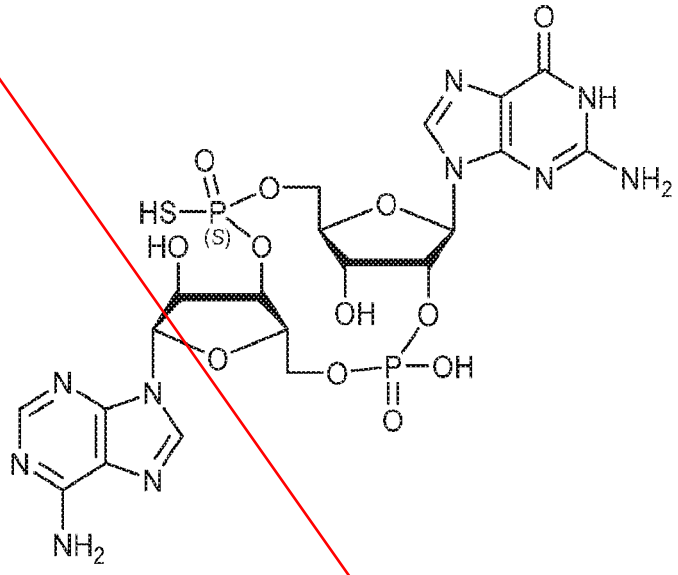
18. A compound according to the formula:



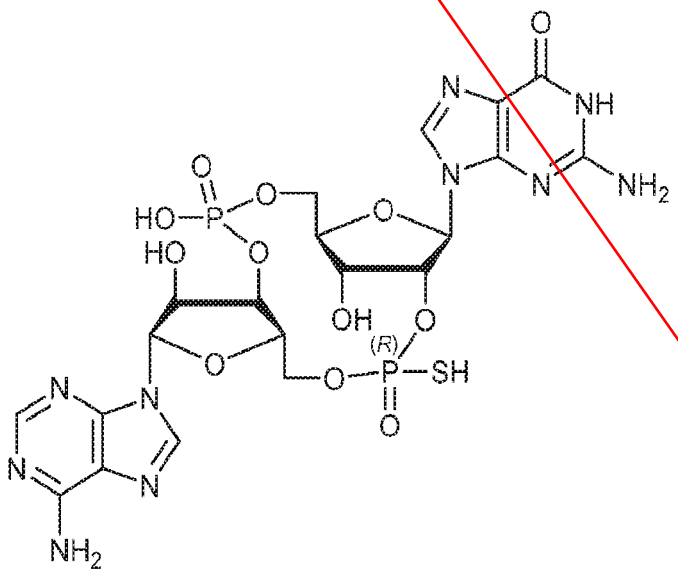
19. A compound according to the formula:



20. A compound according to the formula:



21. A compound according to the formula:



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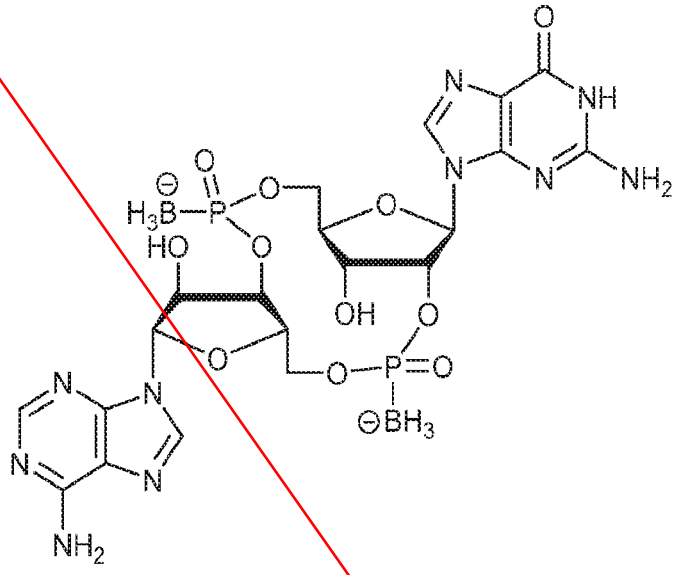

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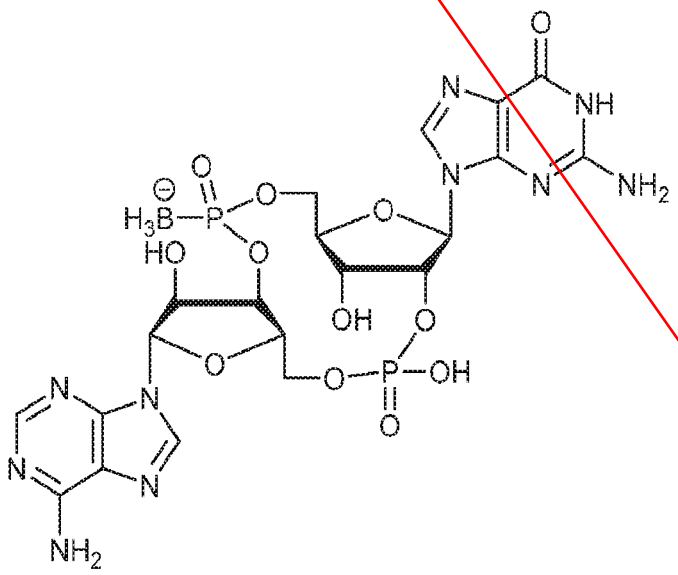
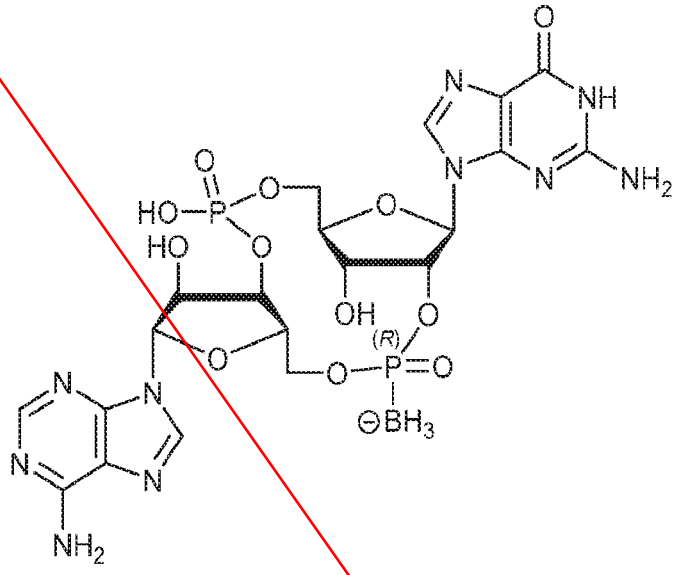


24. A compound according to the formula:



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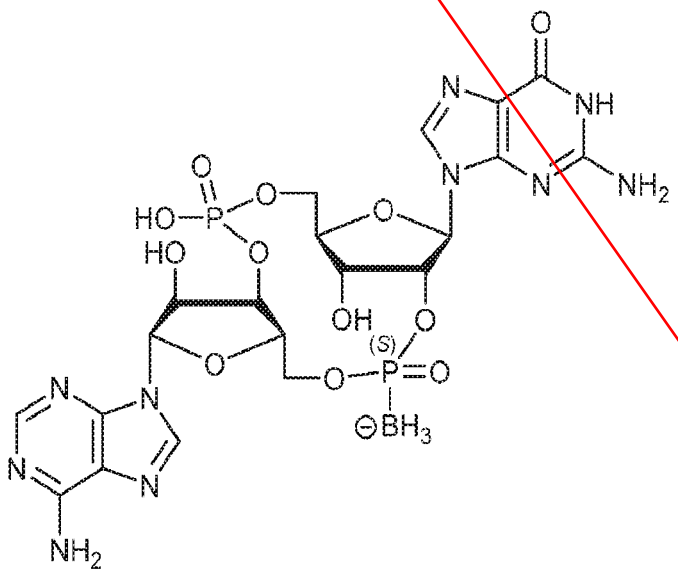
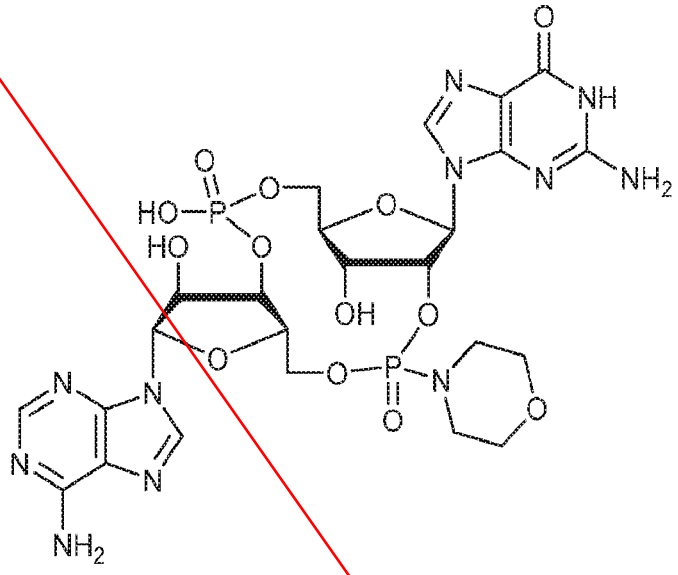
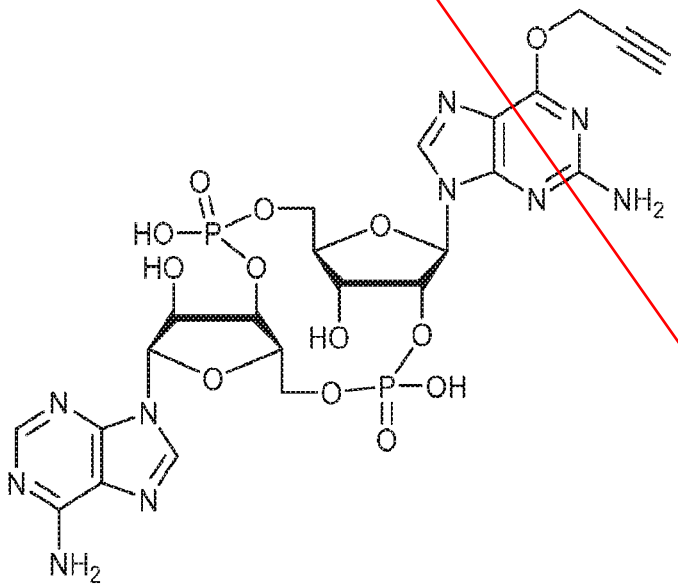


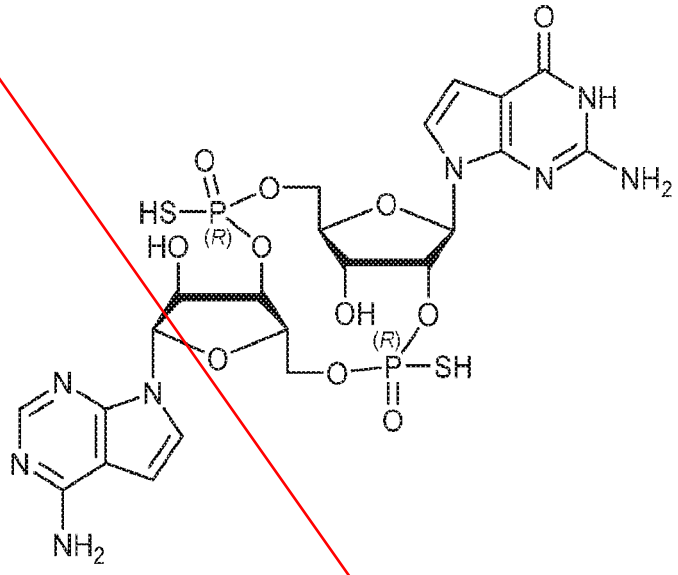
26. A compound according to the formula:



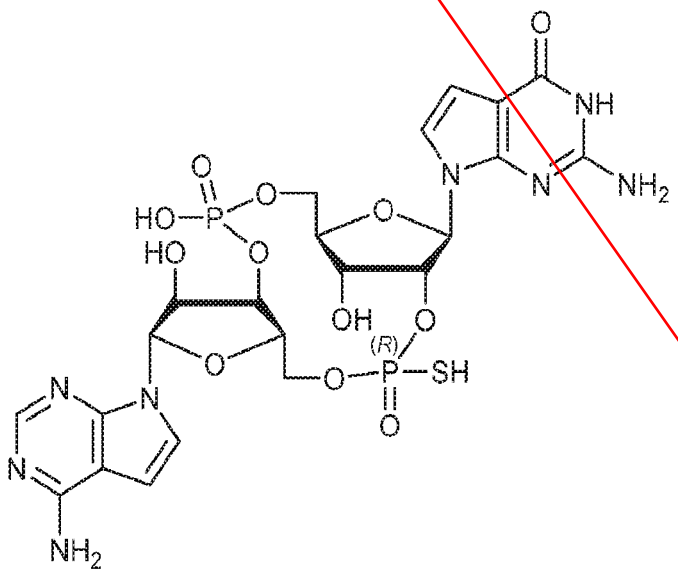
27. A compound according to the formula:



28. A compound according to the formula:



29. A compound according to the formula:



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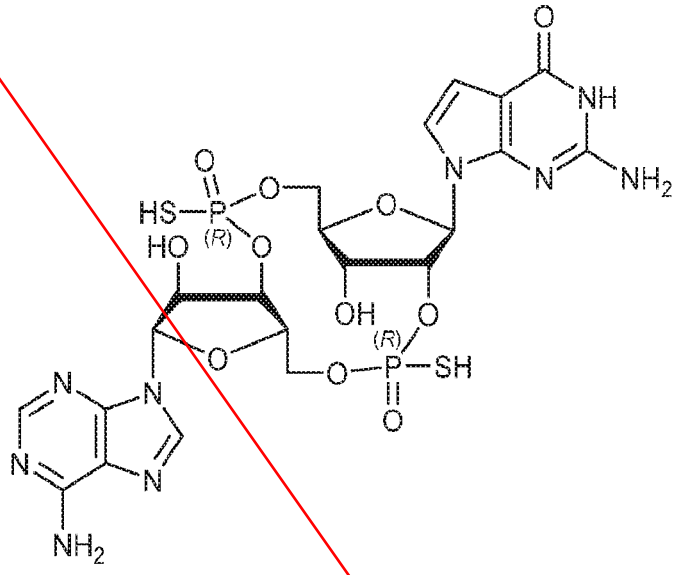

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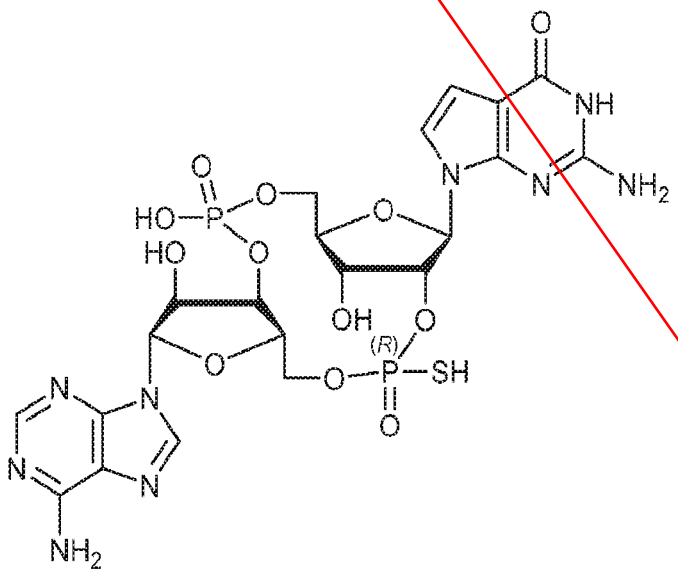

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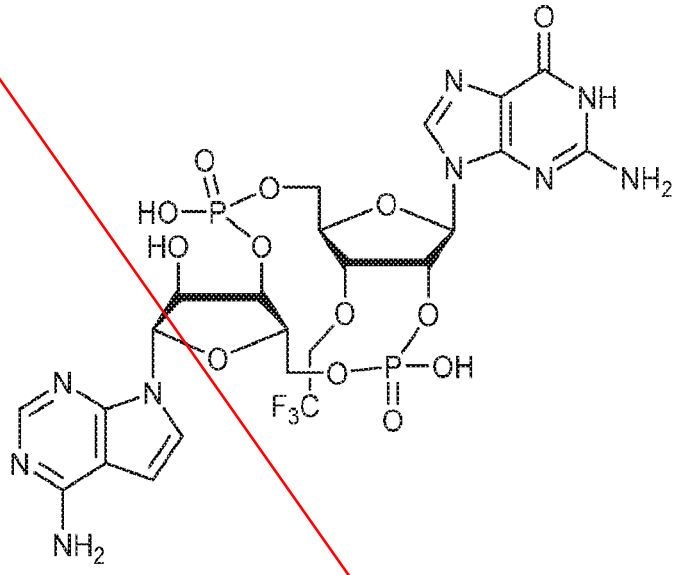
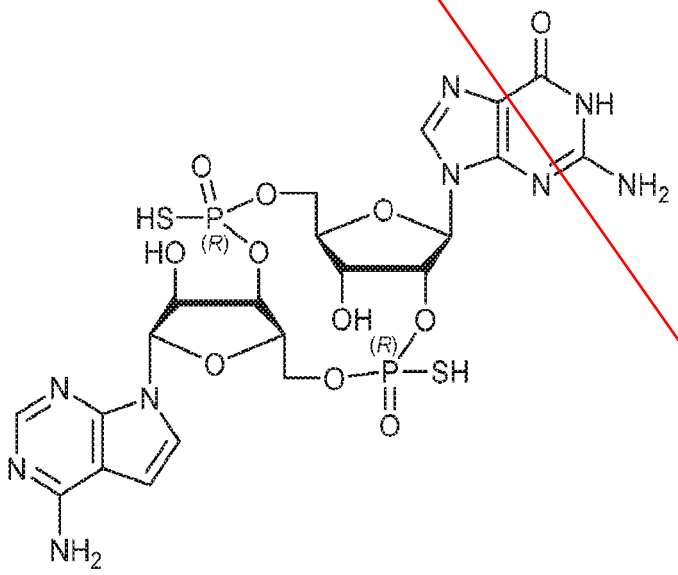
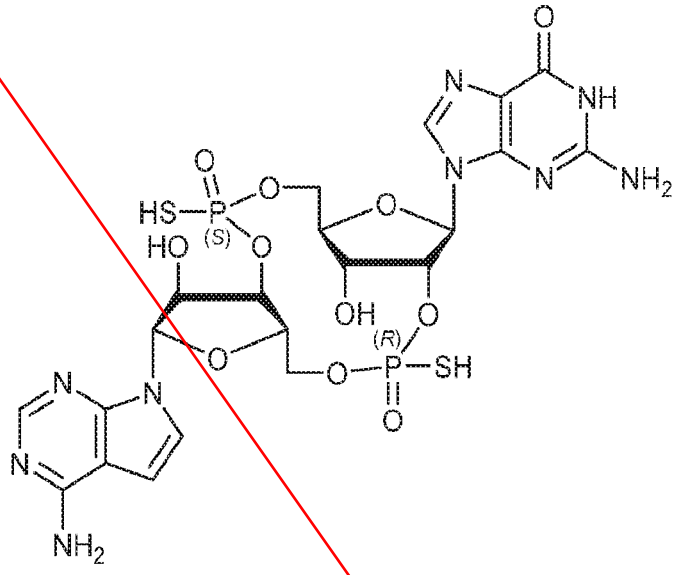


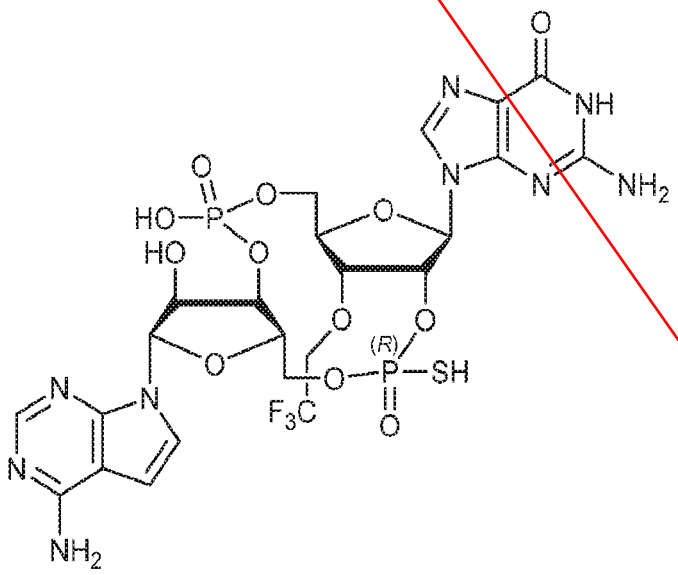
33. A compound according to the formula:



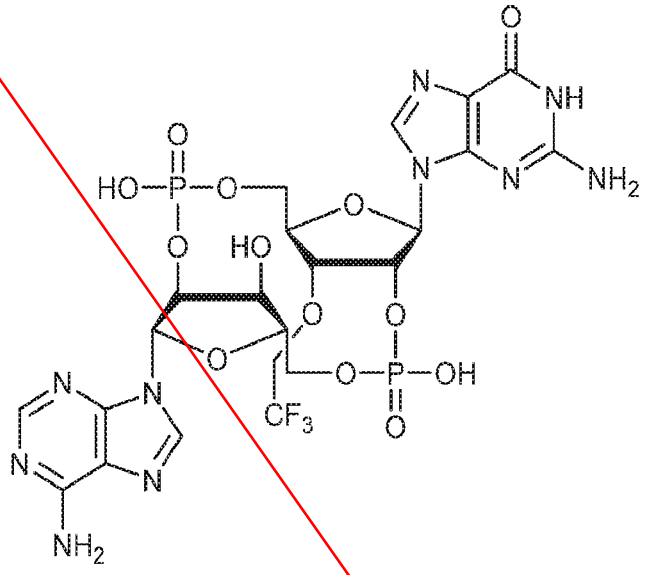
34. A compound according to the formula:



35. A compound according to the formula:



36. A compound according to the formula:



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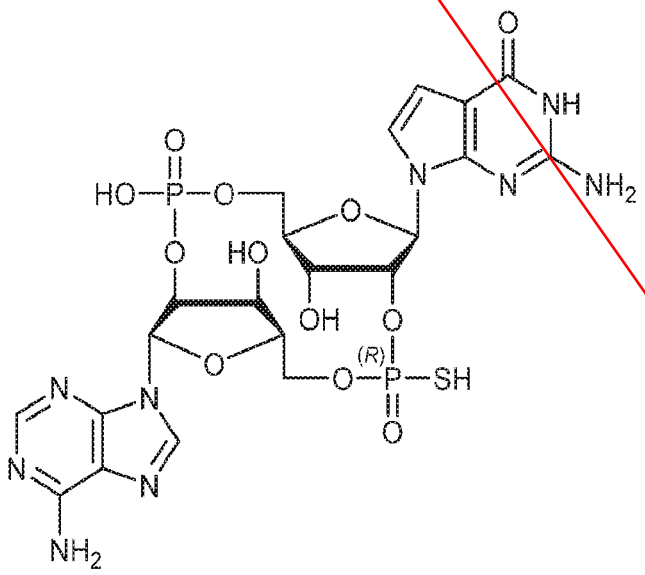
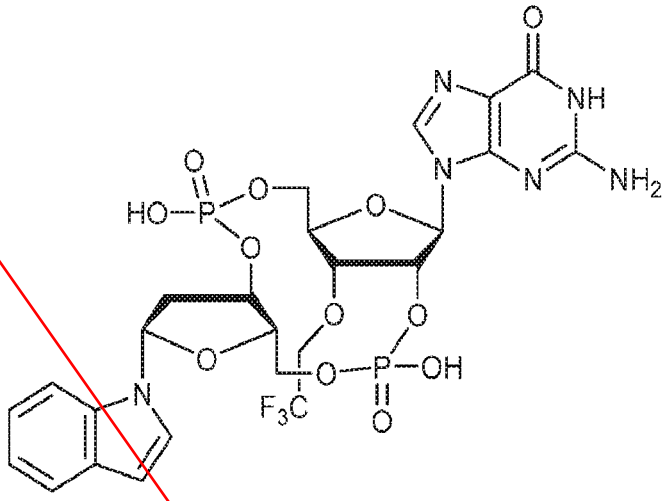


38. A compound selected from the group consisting of:



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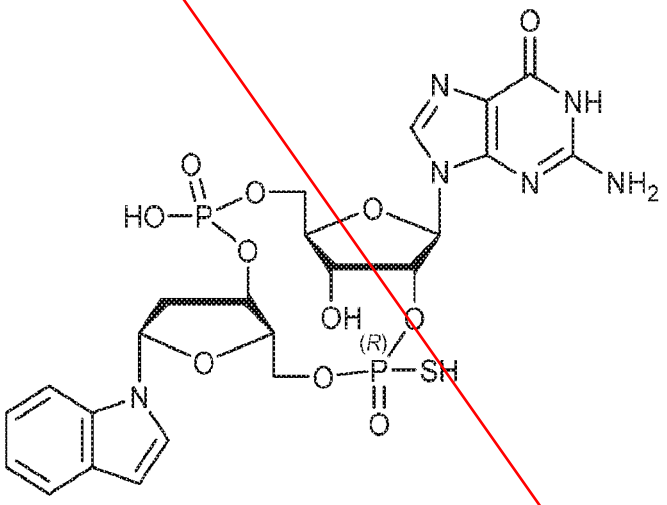

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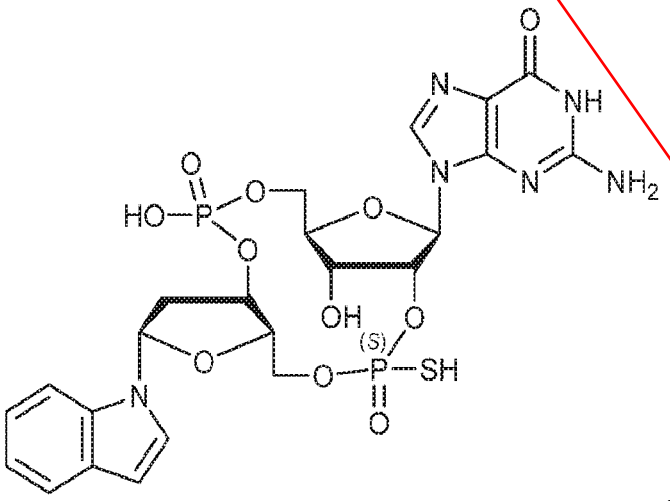

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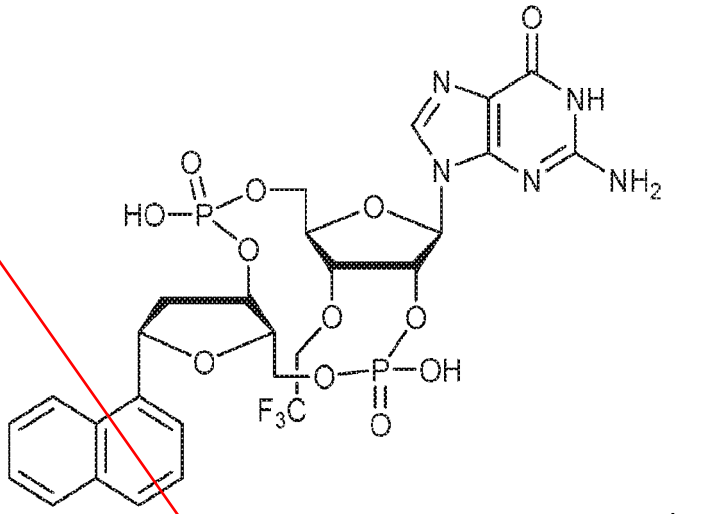

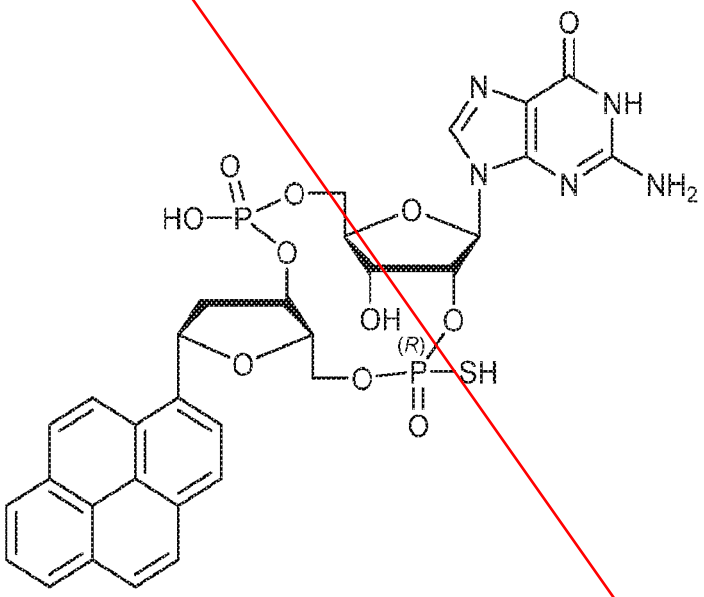

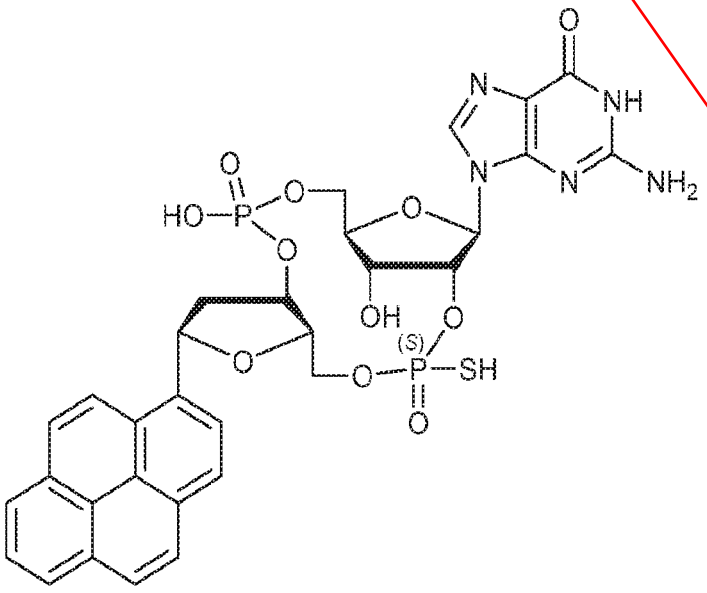

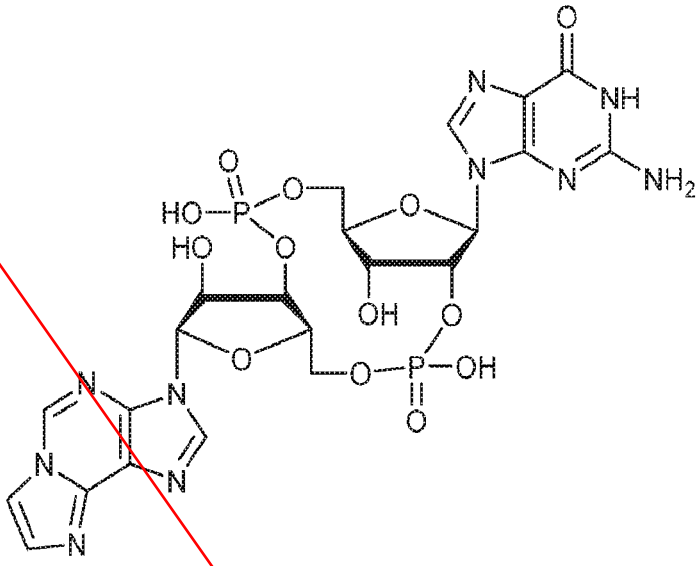

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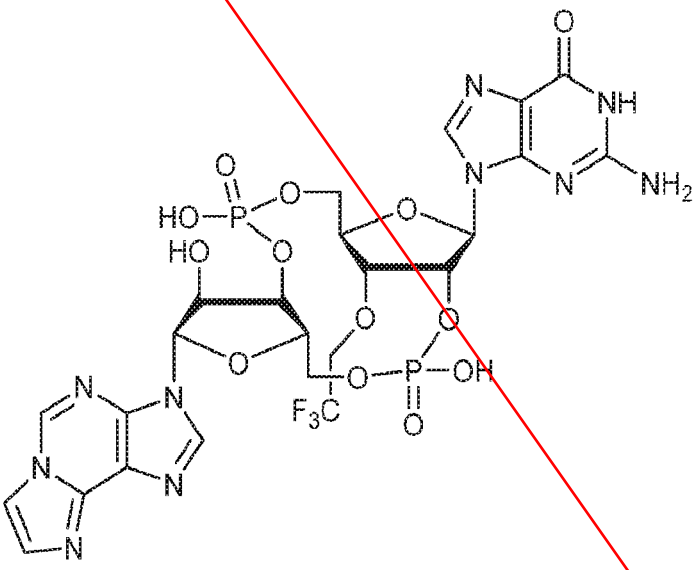

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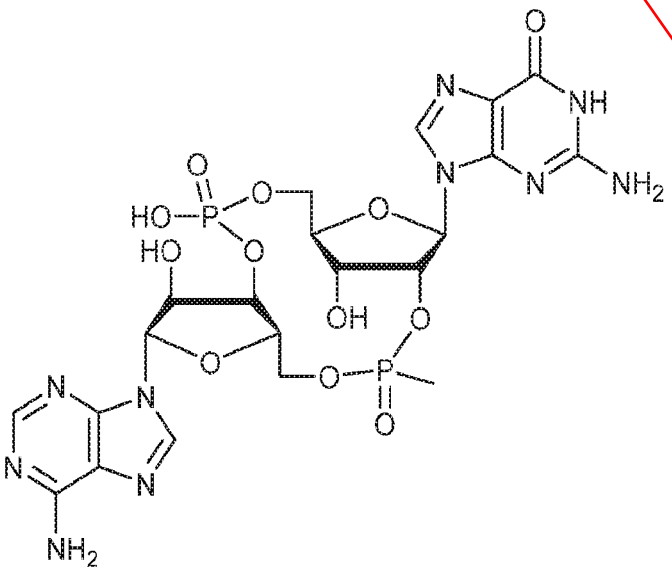

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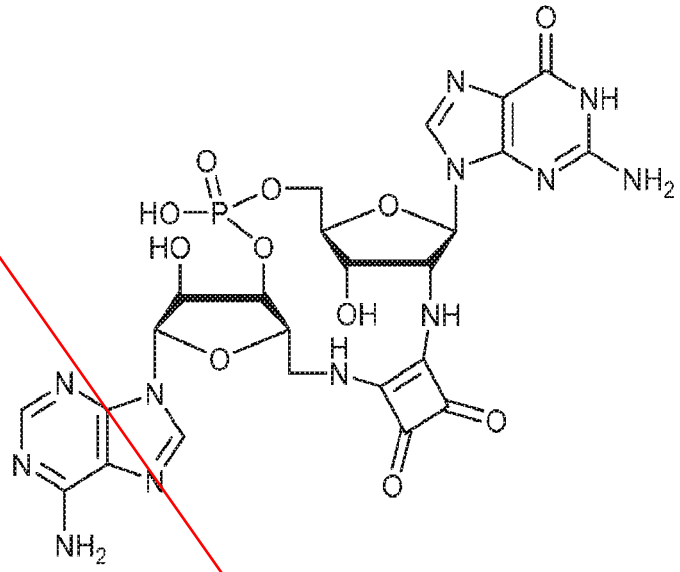

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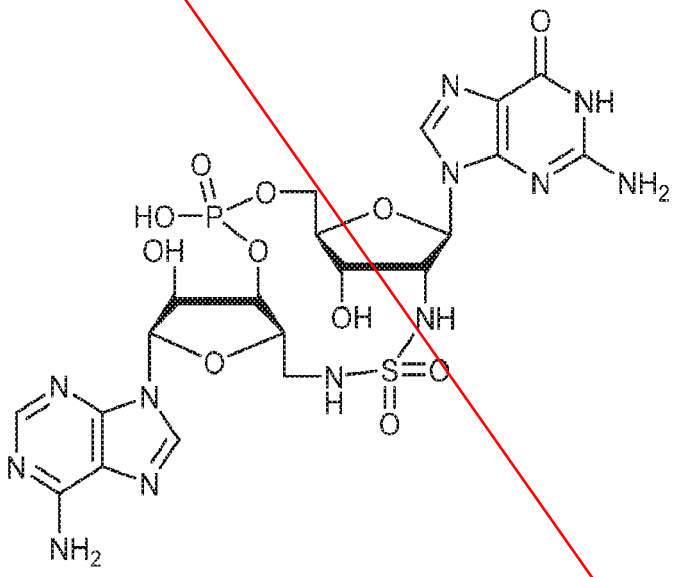
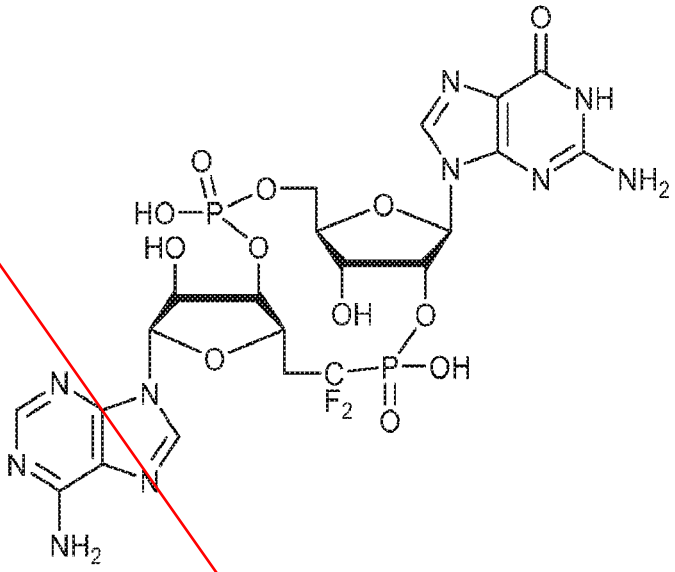


and .

39. A compound selected from the group consisting of:



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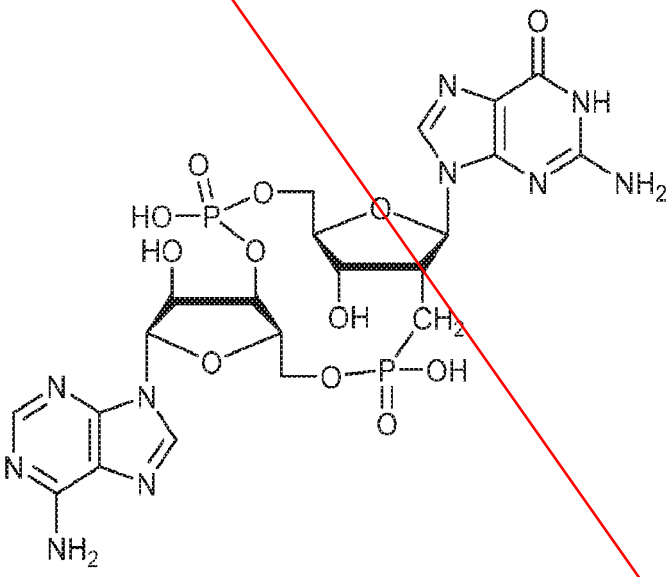

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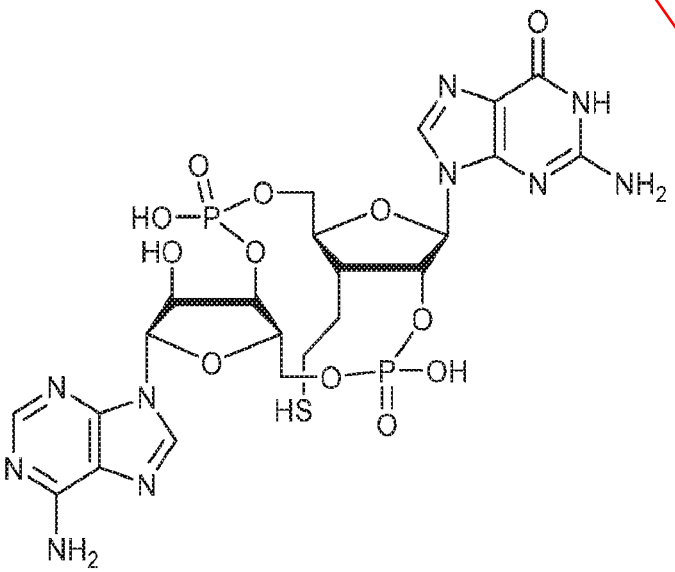

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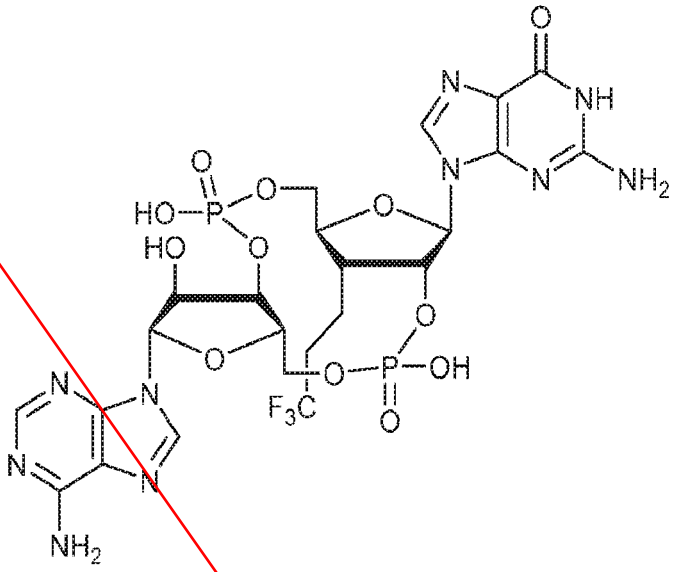

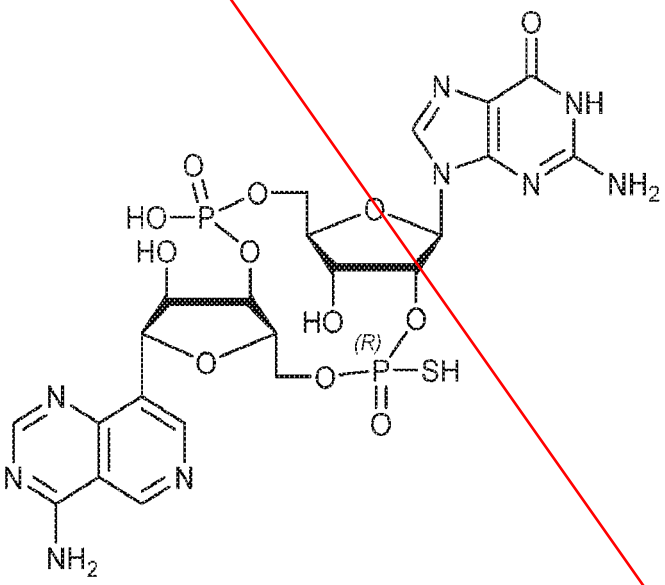

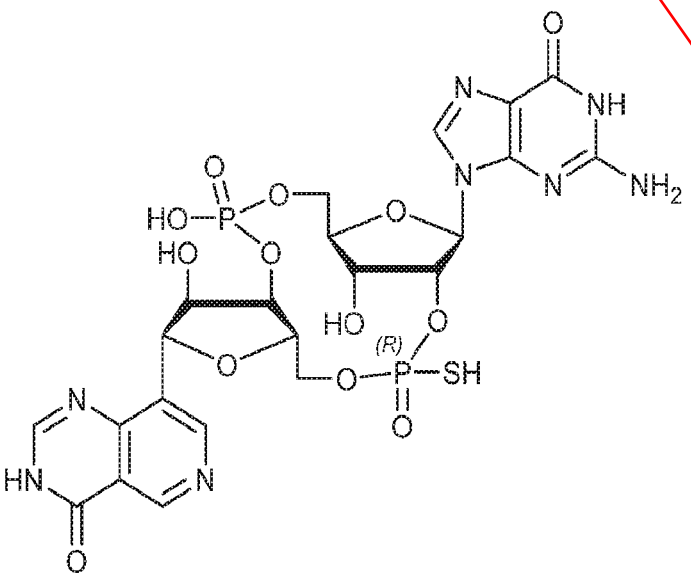

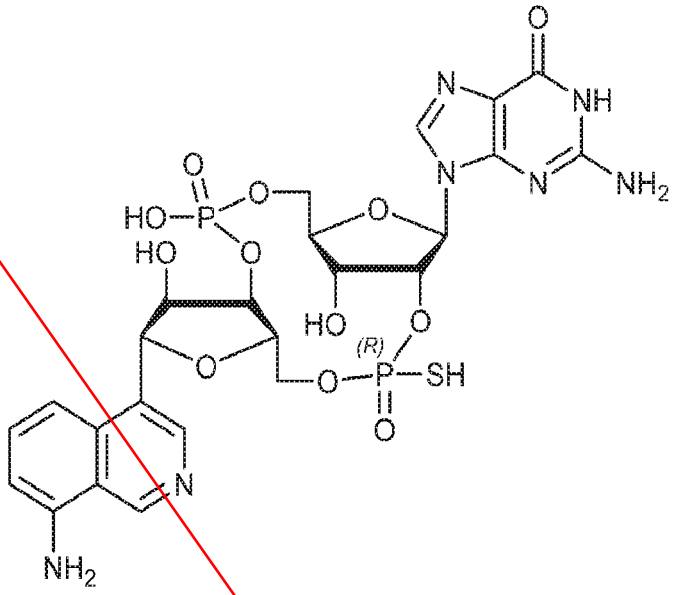

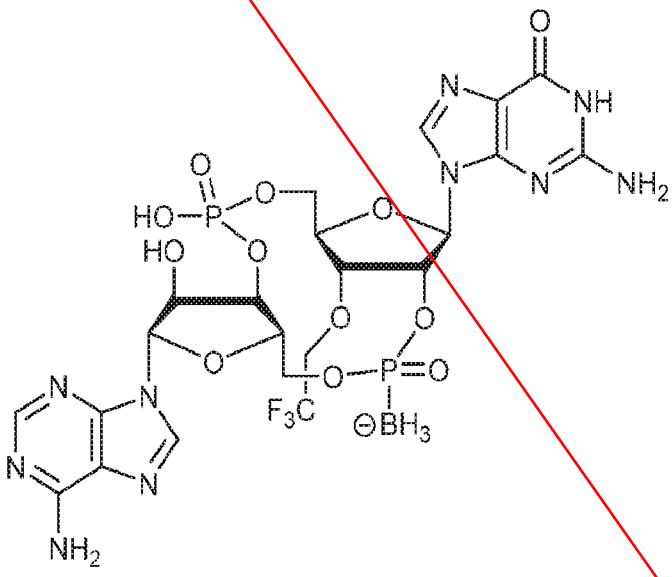

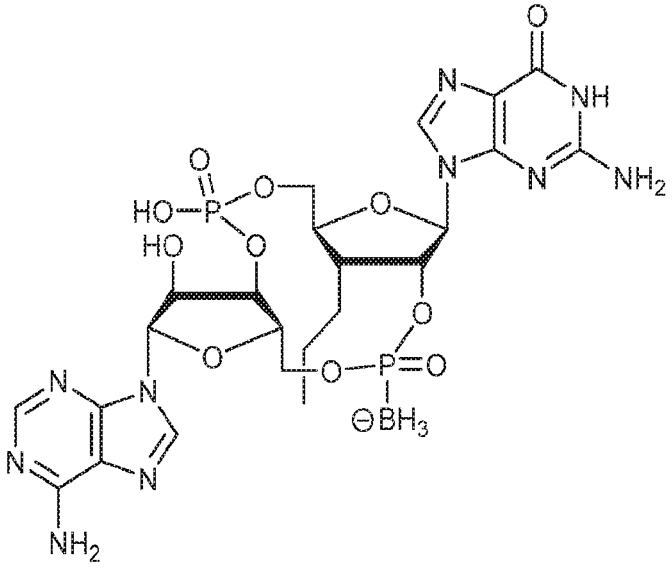

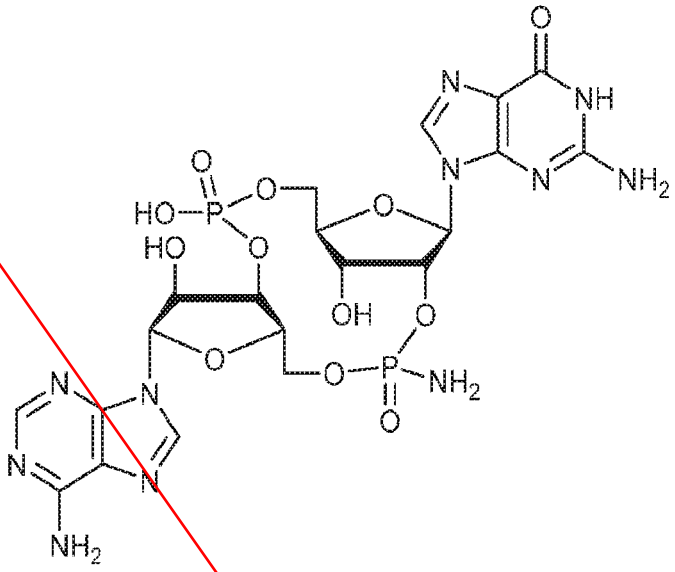

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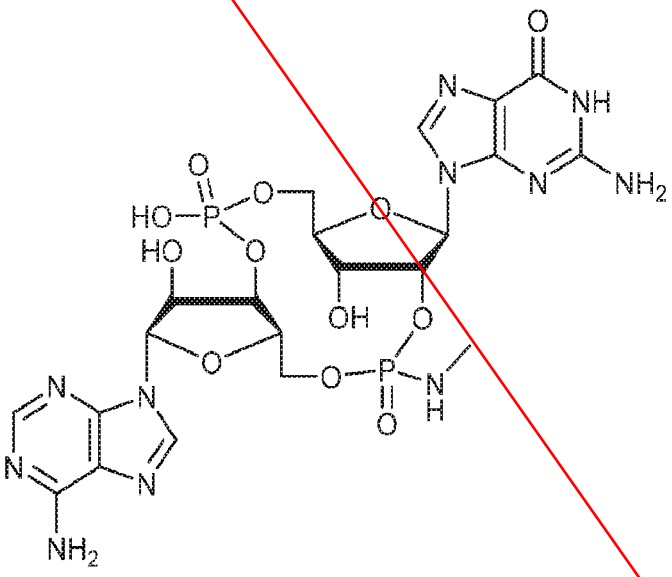

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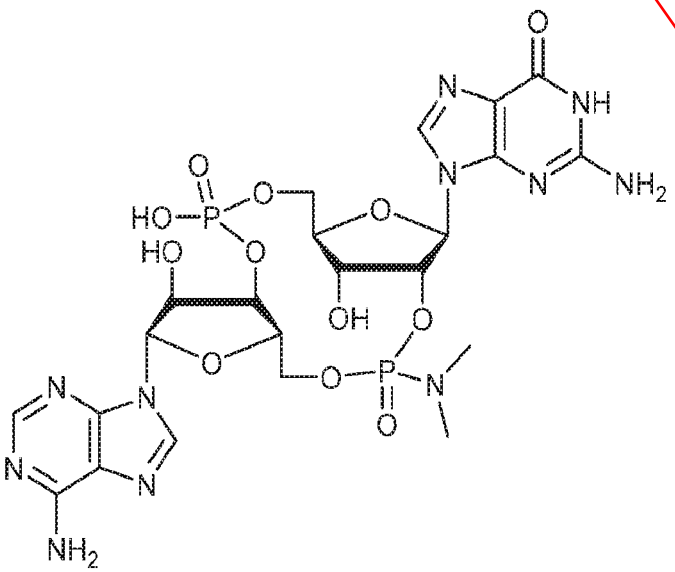

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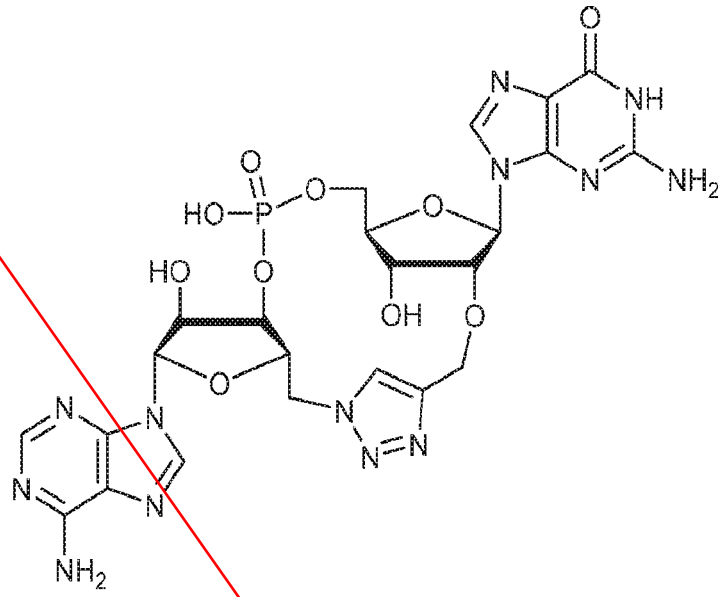
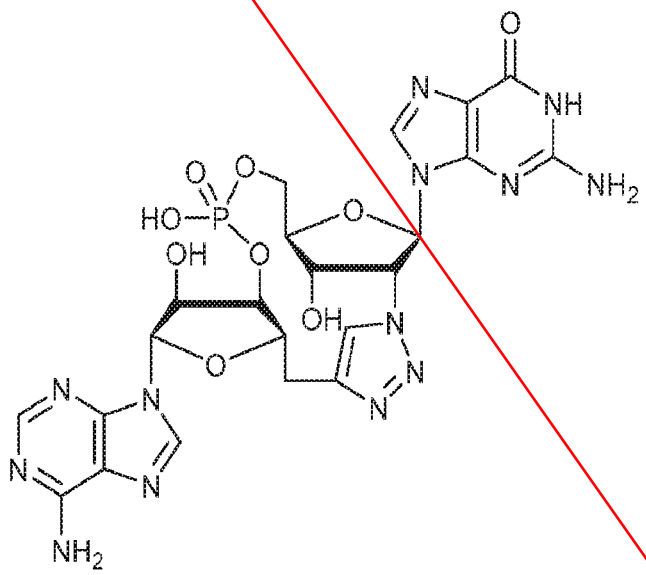
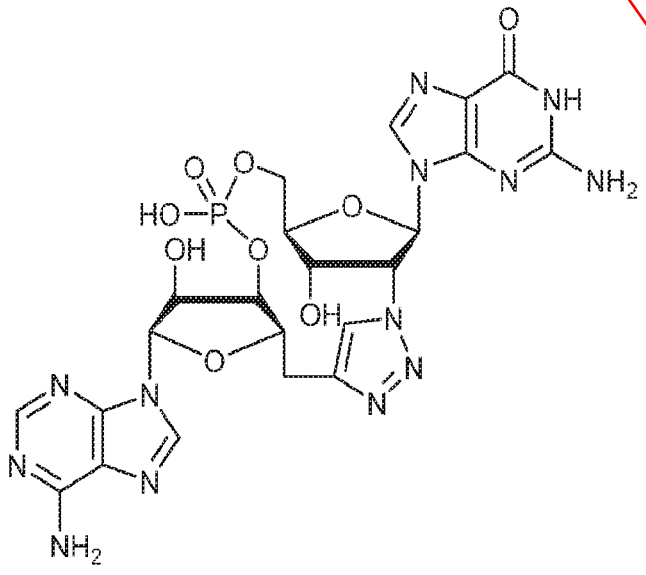
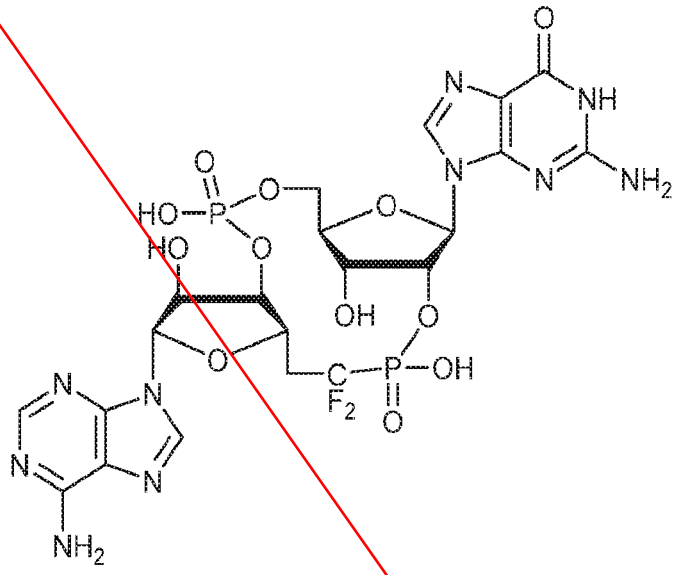




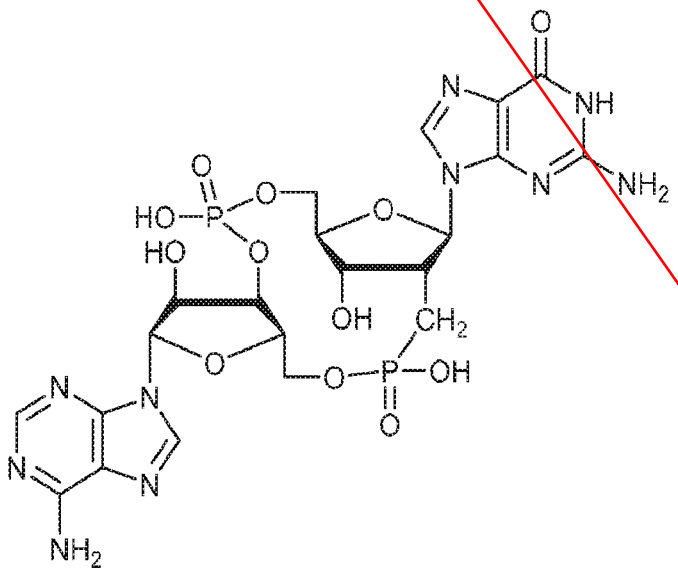


and

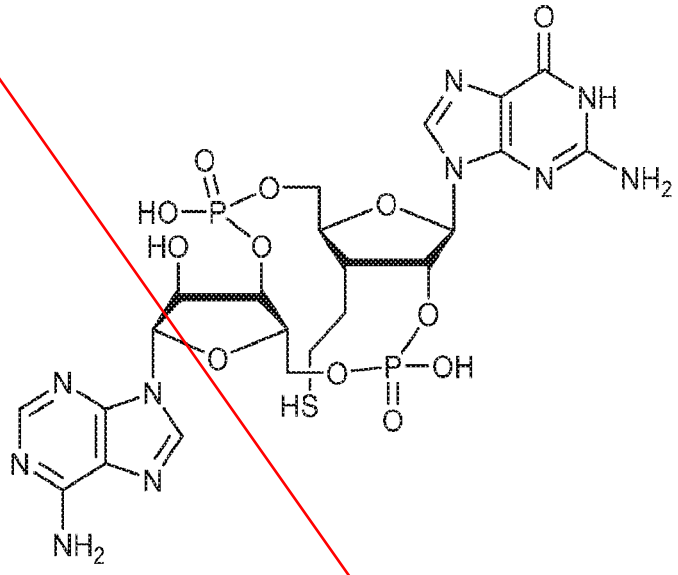
40. A compound according to the formula:



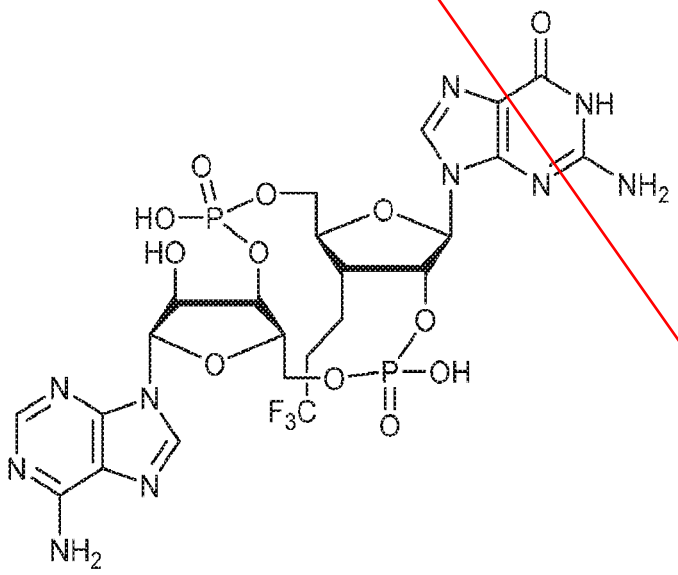
41. A compound according to the formula:



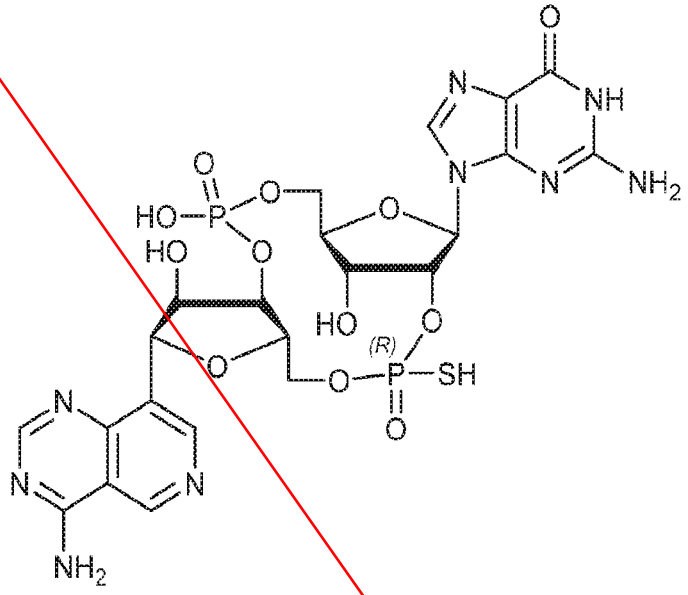
42. A compound according to the formula:



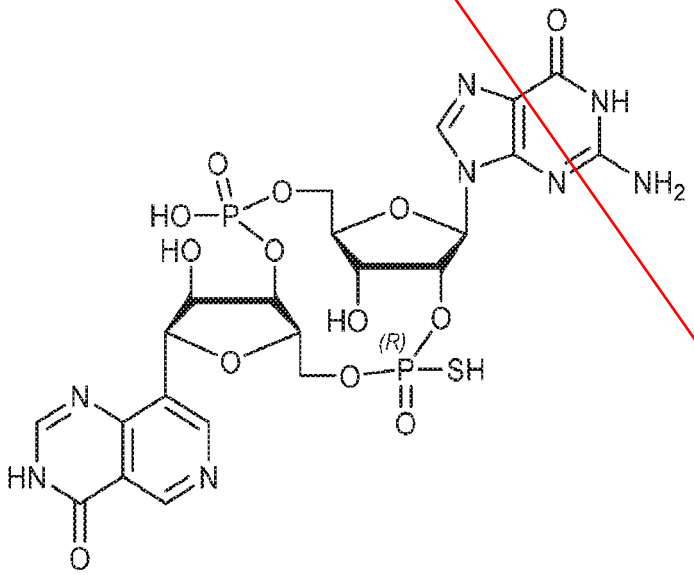
43. A compound according to the formula:



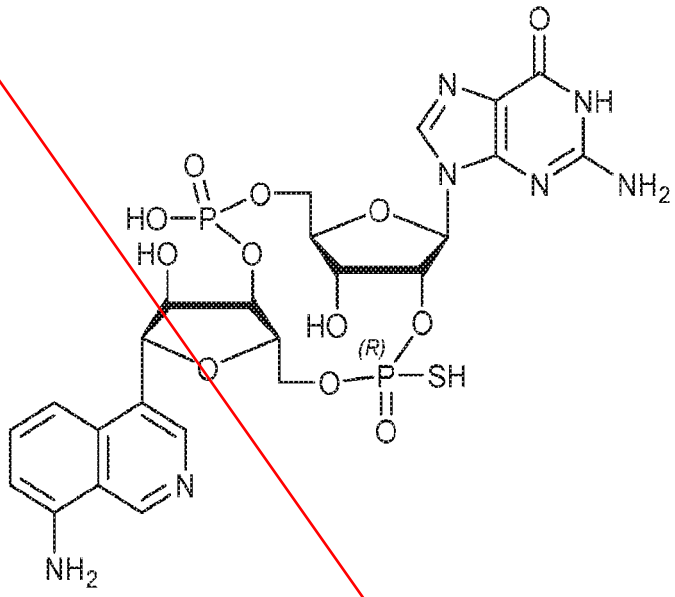
44. A compound according to the formula:



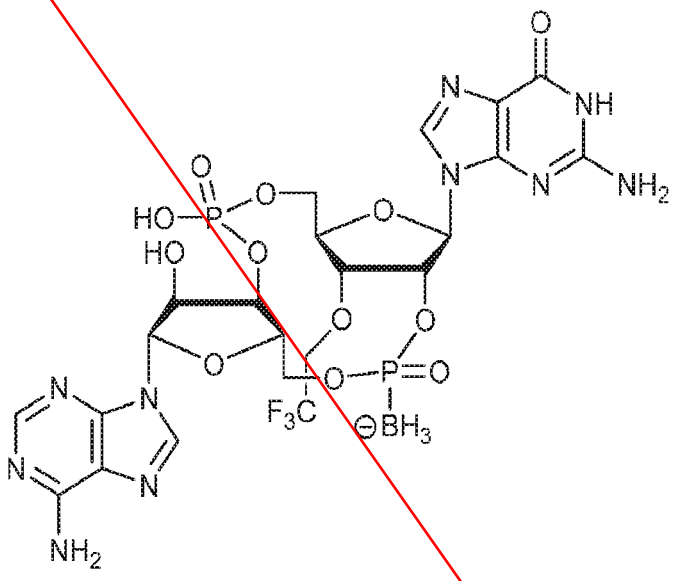
45. A compound according to the formula:



46. A compound according to the formula:

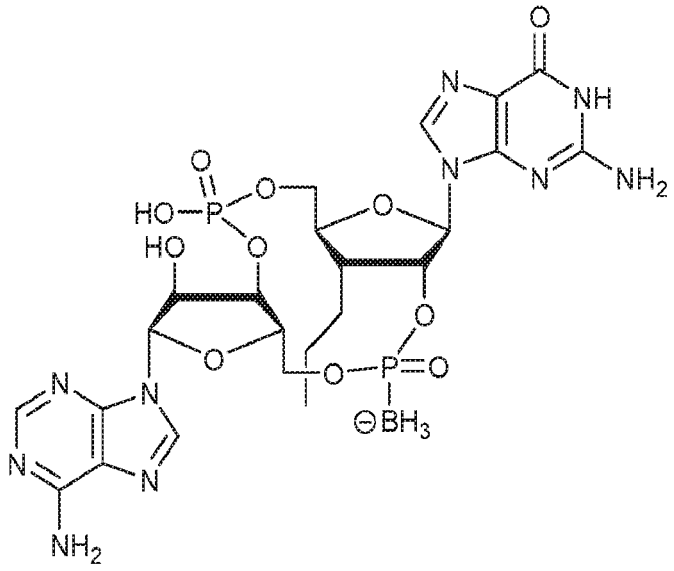


47. A compound selected from the group consisting of ($R_P$)- and ($S_P$)-



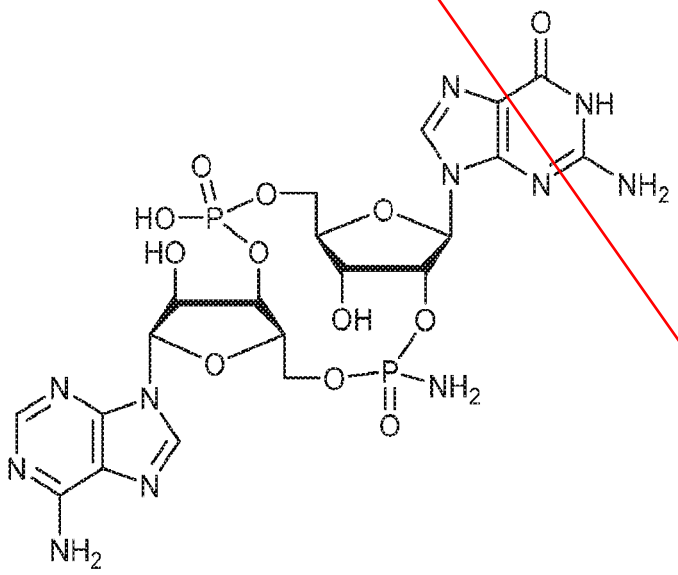
boranophosphates of the formula:

48. A compound selected from the group consisting of ($R_P$)- and ($S_P$)-

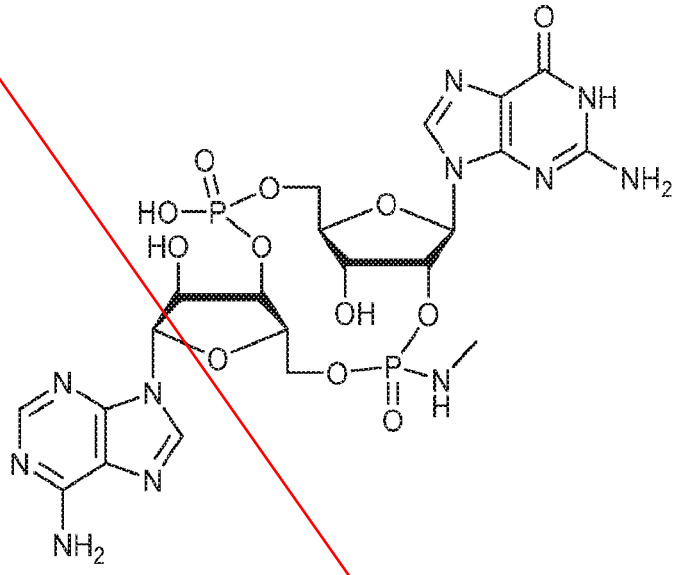


boranophosphates of the formula:

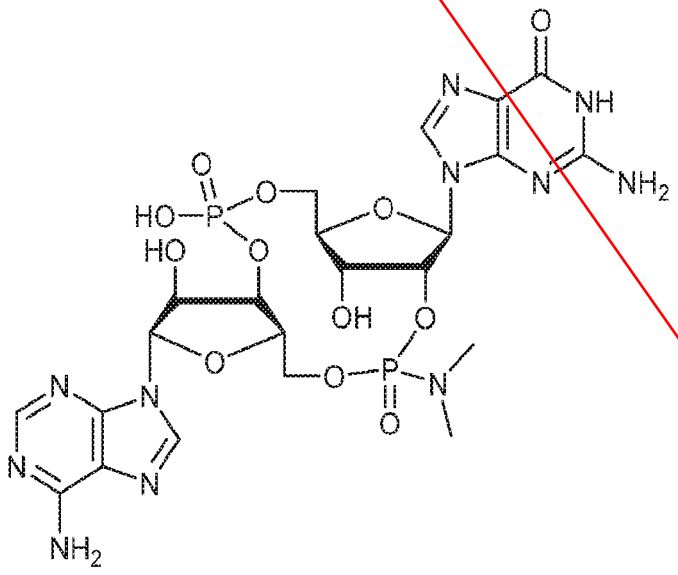
49. A compound according to the formula:



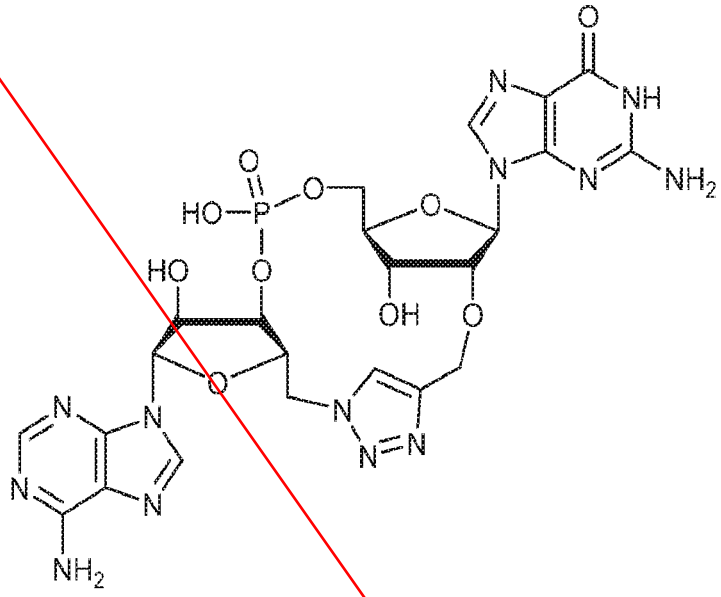
50. A compound according to the formula:



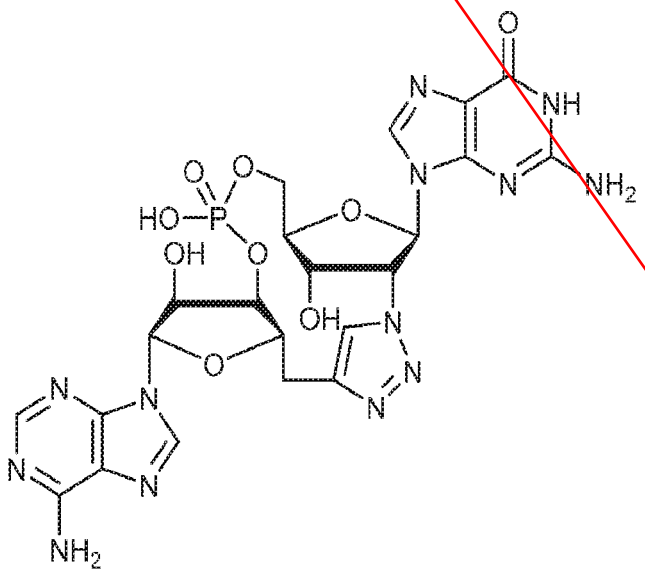
51. A compound according to the formula:



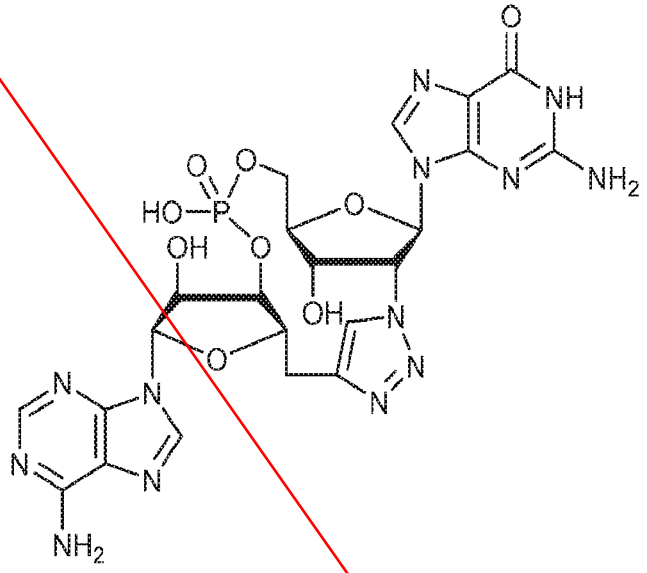
52. A compound according to the formula:



53. A compound according to the formula:



54. A compound according to the formula:



55. A pharmaceutical composition comprising a compound of formula I, or a pharmaceutically acceptable salt thereof.

56. A pharmaceutical composition wherein the composition is a compound of formula I in a pharmaceutical formulation including a nanoparticle or another delivery vehicle.

57. A pharmaceutical composition wherein the composition is a compound of formula I in combination with at least one further therapeutic agent.

58. A pharmaceutical composition of claim 57 wherein the additonal therapeutic agent is an immune checkpoint inhibitor including but is not limited to antibodies against PD-1, PD-L1 or CTLA-4.

59. A pharmaceutical composition of claim 57 wherein the additional therapeutic agent is radiation including stereiotactic body radiation therapy (SBRT).

60. A pharmaceutical composition of claim 57 wherein the additional therapeutic agent is an anti-neoplastic agent, including chemotherapeutic agent and therapeutic antibodies.

61. A pharmaceutical composition wherein the composition is a compound of formula I in a pharmaceutical formulation with an immunogen of a cancer cell (tumor antigen) or of an infectious pathogen.

62. A pharmaceutical composition of claim 57 wherein the composition further comprises one or more of pharmaceutically acceptable carriers, diluents and excipients.

63. A method of inducing or promoting an immune response comprising administering to a patient in need thereof, an effective amount of a compound of formula I, or a pharmaceutically acceptable salt thereof.

64. A method of inducing or promoting an immune response comprising administering to a patient in need thereof, an effective amount of a pharmaceutical composition according to claim 63.

65. A method of inducing or promoting a STING-dependent immune response comprising administering to a patient in need thereof, an effective amount of a compound of formula I, or a pharmaceutically acceptable salt thereof.

66. A method of inducing or promoting a STING-dependent immune response comprising administering to a patient in need thereof, an effective amount of a pharmaceutical composition according to claim 63.

67. A method of treating cancer comprising administering to a patient in need thereof, a therapeutically effective amount of a compound of formula **I**, or a pharmaceutically acceptable salt thereof.

68. A method of treating cancer comprising administering to a patient in need thereof, a therapeutically effective amount of a pharmaceutical composition according to claim 67.

69. A method of treating cancer comprising administering to a patient in need thereof, a therapeutically effective amount of a pharmaceutical composition comprising a compound of formula **I**, or a pharmaceutically acceptable salt thereof, in combination with immune checkpoint antibodies, including but is not limited to, antibodies against PD-1, PD-L1 or CTLA-4.

70. A method of treating cancer comprising administering to a patient in need thereof, a therapeutically effective amount of a pharmaceutical composition comprising a compound of formula **I**, or a pharmaceutically acceptable salt thereof, in combination with radiation including stereiotactic body radiation therapy (SBRT).

71. A method of treating cancer comprising administering to a patient in need thereof, a therapeutically effective amount of a pharmaceutical composition comprising a compound of formula **I**, or a pharmaceutically acceptable salt thereof, in combination with an anti-neoplastic agent, including chemotherapeutic agent and therapeutic antibodies.

72. A method of treating infectious diseases comprising administering to a patient in need thereof, a therapeutically effective amount of a compound of formula **I**, or a pharmaceutically acceptable salt thereof.

73. A method of treating infectious diseases comprising administering to a patient in need thereof, a therapeutically effective amount of a pharmaceutical composition according to claims 72.

74. A method of treating immune disorders comprising administering to a patient in need thereof, a therapeutically effective amount of a compound of formula **I**, or a pharmaceutically acceptable salt thereof.

75. A method of treating immune disorders comprising administering to a patient in need thereof, a therapeutically effective amount of a pharmaceutical composition according to claims 74.

76. A vaccine composition comprising an antigen or antigen composition and a compound of Formula **I**, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of a disease.

77. The use of a compound of Formula **I**, or a pharmaceutically acceptable salt thereof, for the manufacture of a vaccine composition comprising an antigen or antigen composition for the treatment or prevention of a disease.

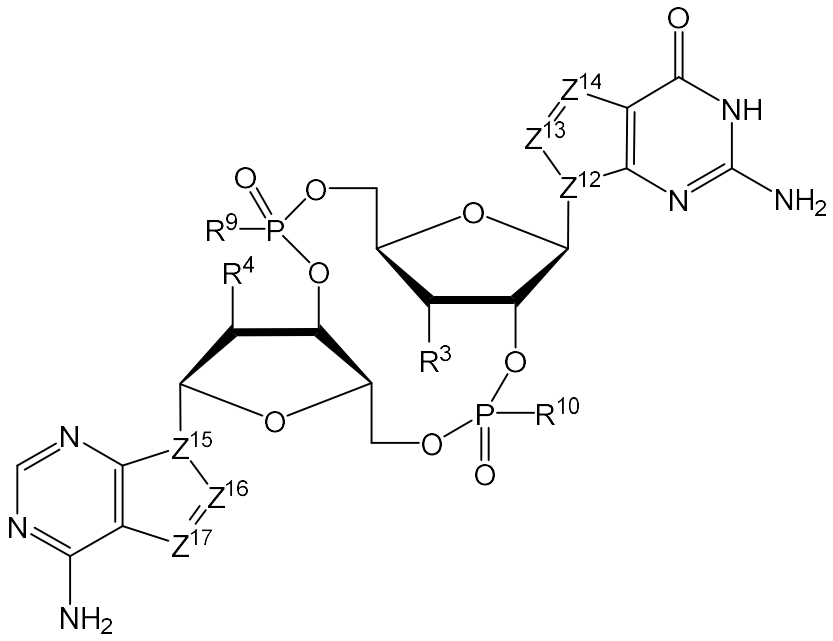
78. A method of treating or preventing a disease comprising the administration to a patient suffering from or susceptible to the disease, a vaccine composition comprising an antigen or antigen composition and a compound of Formula **I**, or a pharmaceutically acceptable salt thereof.

79. A method of treating or preventing a disease comprising administering to a patient in need thereof, a therapeutically effective amount of a compound of formula **I**, or a pharmaceutically acceptable salt thereof, wherein the patient is a mammal.

80. A method of treating or preventing a disease comprising administering to a patient in need thereof, a therapeutically effective amount of a compound of formula I, or a pharmaceutically acceptable salt thereof, wherein the patient is a human.

**CLAIMS**

1. A compound, wherein the compound is of Formula Ic:



Formula Ic

wherein

$Z^{12}$ and $Z^{15}$ are N;

$Z^{13}$, $Z^{14}$, $Z^{16}$, and $Z^{17}$ are independently CH or N;

$R^3$ is $C_2$alkyl functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, di($C_{1\text{-}6}$alkyl)amino, or azido groups;

$R^4$ is hydroxyl;

$R^9$ and $R^{10}$ are independently hydroxyl; thiol; $C_{1\text{-}6}$alkyl; $C_{1\text{-}6}$alkyl functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, di($C_{1\text{-}6}$alkyl)amino, or azido groups; $C_{1\text{-}6}$alkoxy; $C_{1\text{-}6}$alkoxy functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino, di($C_{1\text{-}6}$alkyl)amino, or azido groups; $C_{3\text{-}5}$alkenyl-O-; $C_{3\text{-}5}$alkynyl-O-; oligo(ethylene glycol); poly(ethylene glycol); borano ($-BH_3^-$); or $-NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen; $C_{1\text{-}6}$alkyl; $C_{1\text{-}6}$alkyl functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$hydroxyalkoxy, amino, $C_{1\text{-}6}$alkylamino,

di($C_{1-6}$alkyl)amino, or azido groups; cyclic -($C_{1-6}$alkyl)-; cyclic -($C_{1-6}$alkyl)- functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups; cyclic -($C_{1-6}$oxaalkyl)-; or cyclic -($C_{1-6}$oxaalkyl)- functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;
or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein $Z^{13}$ and $Z^{16}$ are CH.

3. The compound of claim 1, wherein $Z^{14}$ and $Z^{17}$ are N.

4. The compound of claim 1, wherein $Z^{13}$ and $Z^{16}$ are CH, and $Z^{14}$ and $Z^{17}$ are N.

5. The compound of claim 1, wherein $R^9$ and $R^{10}$ are independently hydroxyl or thiol.

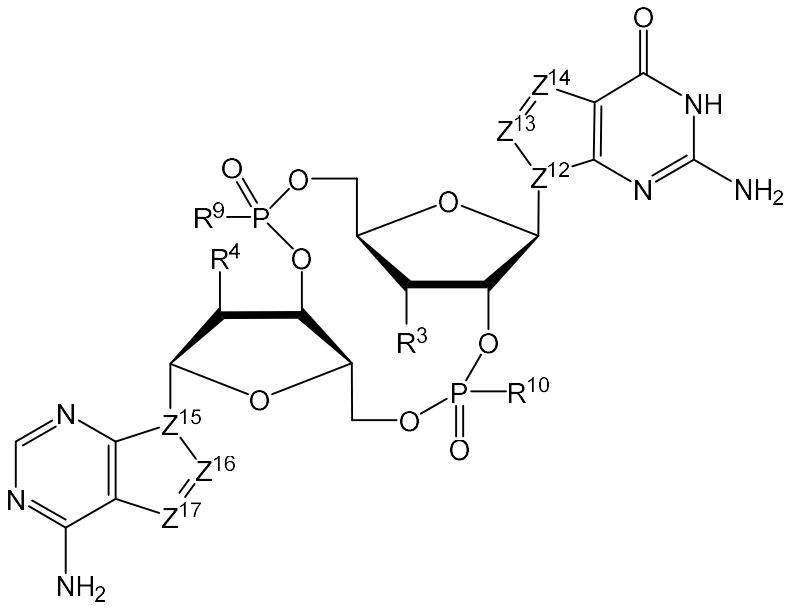
6. The compound of claim 1, wherein $R^9$ and $R^{10}$ are hydroxyl.

7. The compound of claim 1, wherein $R^9$ and $R^{10}$ are thiol.

8. The compound of claim 1, wherein $R^3$ is $C_2$alkyl functionalized with one or more thiol, hydroxyl, carboxyl, $C_{1-6}$hydroxyalkoxy, amino, or $C_{1-6}$alkylamino groups.

9. The compound of claim 1, wherein $R^3$ is $C_2$alkyl functionalized with one or more halogen, thiol, or hydroxyl.

10. A compound, wherein the compound is of Formula Ic:



Formula Ic

wherein

$Z^{12}$ and $Z^{15}$ are N;

$Z^{13}$ and $Z^{16}$ are CH;

$Z^{14}$ and $Z^{17}$ are independently CH or N;

$R^3$ is $C_2$alkyl functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups;

$R^4$ is hydroxyl;

$R^9$ and $R^{10}$ are independently hydroxyl or thiol;

or a pharmaceutically acceptable salt thereof.

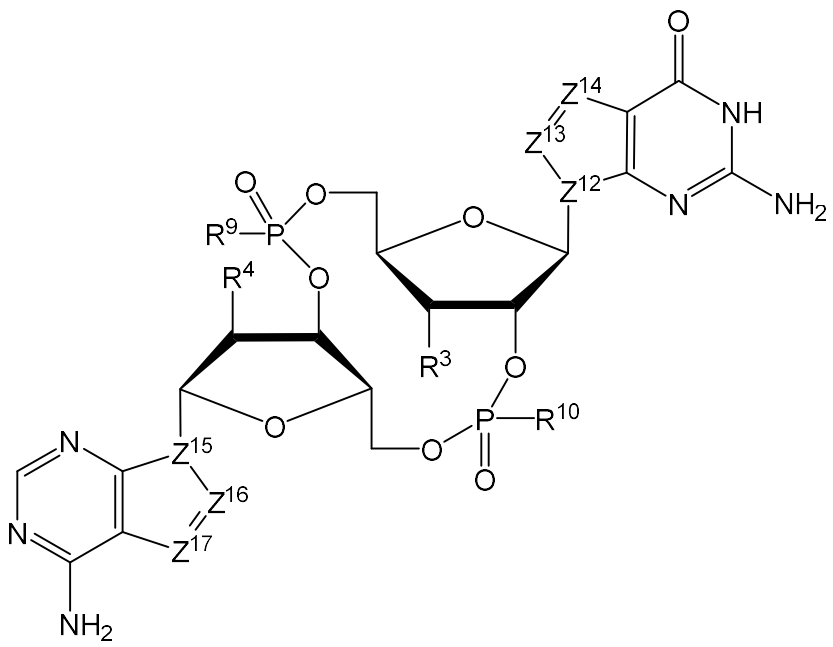
11. The compound of claim 10, wherein $R^3$ is $C_2$alkyl functionalized with one or more thiol, hydroxyl, carboxyl, $C_{1-6}$hydroxyalkoxy, amino, or $C_{1-6}$alkylamino groups.

12. The compound of claim 10, wherein $R^3$ is $C_2$alkyl functionalized with hydroxyl.

13. The compound of claim 10, wherein $R^3$ is $C_2$alkyl functionalized with thiol.

14. The compound of claim 10, wherein $R^3$ is $C_2$alkyl functionalized with halogen.

15. A compound, wherein the compound is of Formula Ic:



Formula Ic

wherein

$Z^{12}$ and $Z^{15}$ are N;

$Z^{13}$, $Z^{14}$, $Z^{16}$, and $Z^{17}$ are independently CH or N;

$R^3$ is $C_{1-6}$alkyl functionalized with one or more halogen, thiol, or hydroxyl;

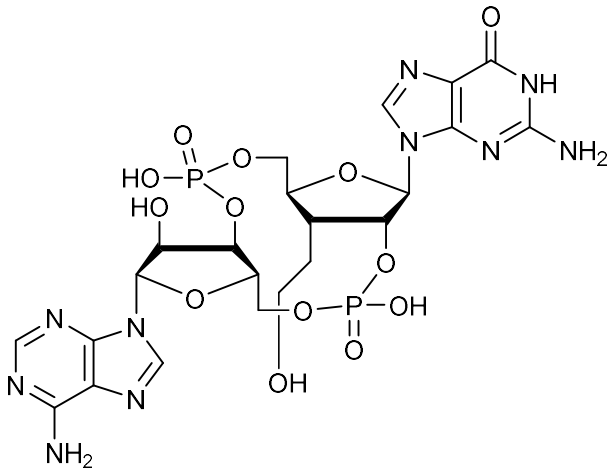
$R^4$ is hydroxyl;

$R^9$ and $R^{10}$ are independently hydroxyl; thiol; $C_{1-6}$alkyl; $C_{1-6}$alkyl functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups; $C_{1-6}$alkoxy; $C_{1-6}$alkoxy functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups; $C_{3-5}$alkenyl-O-; $C_{3-5}$alkynyl-O-; oligo(ethylene glycol); poly(ethylene glycol); borano ($-BH_3^-$); or $-NR^7R^8$;

$R^7$ and $R^8$ are independently hydrogen; $C_{1-6}$alkyl; $C_{1-6}$alkyl functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, di($C_{1-6}$alkyl)amino, or azido groups; cyclic -($C_{1-6}$alkyl)-; cyclic -($C_{1-6}$alkyl)- functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1-6}$alkoxy, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups; cyclic -($C_{1-6}$oxaalkyl)-; or cyclic -($C_{1-6}$oxaalkyl)-

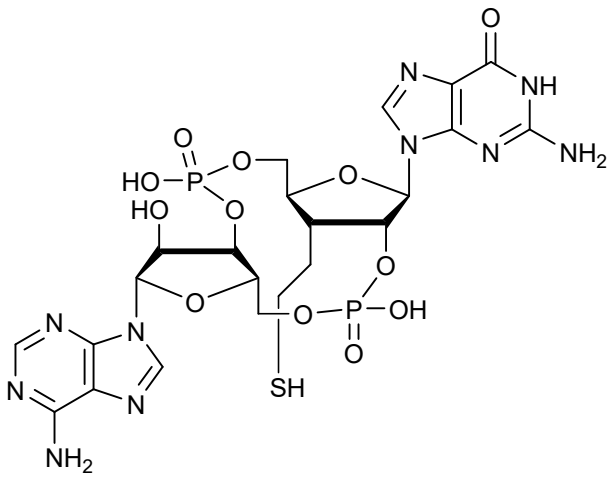
functionalized with one or more halogen, thiol, hydroxyl, carboxyl, $C_{1-6}$hydroxyalkoxy, amino, $C_{1-6}$alkylamino, or di($C_{1-6}$alkyl)amino groups;
or a pharmaceutically acceptable salt thereof.

16. The compound of claim 15 having the structure:



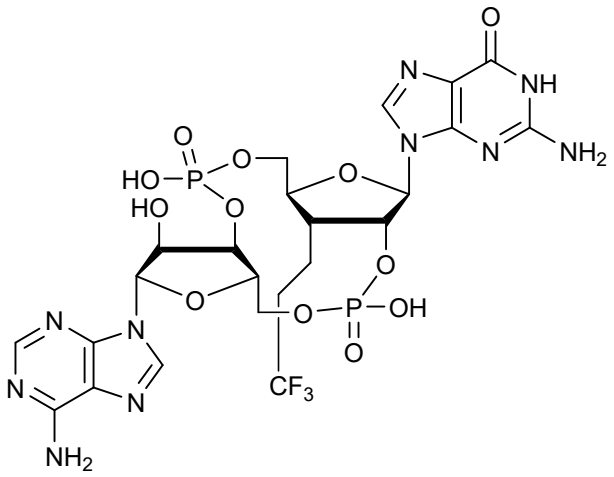
or a pharmaceutically acceptable salt thereof.

17. The compound of claim 15 having the structure:



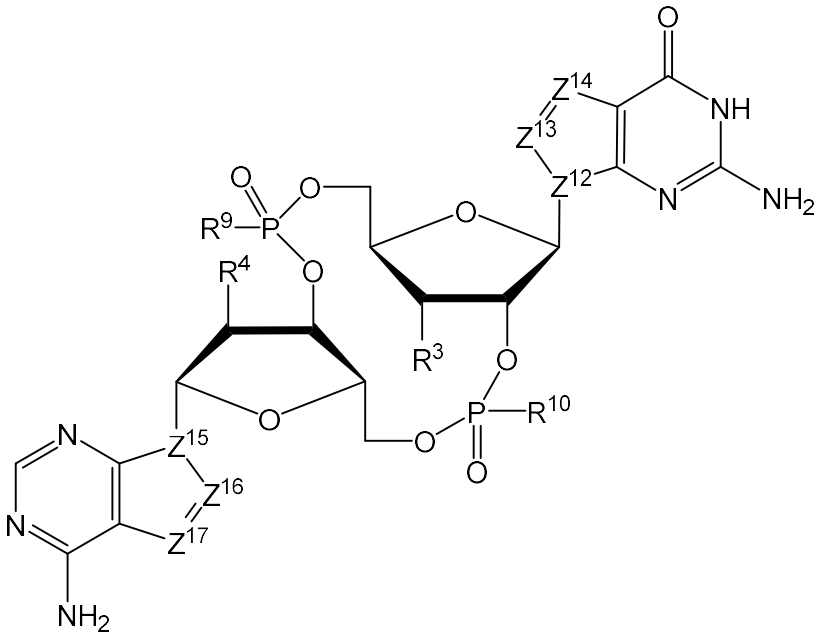
or a pharmaceutically acceptable salt thereof.

18. The compound of claim 15 having the structure:



or a pharmaceutically acceptable salt thereof.

19. A compound, wherein the compound is of Formula Ic:



Formula Ic

wherein

$Z^{12}$ and $Z^{15}$ are N;

$Z^{13}$ and $Z^{16}$ are CH;

$Z^{14}$ and $Z^{17}$ are independently CH or N;

$R^3$ is $C_{1-6}$alkyl functionalized with one or more halogen, thiol, or hydroxyl;

$R^4$ is hydroxyl;

$R^9$ and $R^{10}$ are independently hydroxyl or thiol;

or a pharmaceutically acceptable salt thereof.

20. The compound of claim 19, wherein $R^3$ is $C_{1-6}$alkyl functionalized with hydroxyl.

21. The compound of claim 19, wherein $R^3$ is $C_{1-6}$alkyl functionalized with thiol.

22. The compound of claim 19, wherein $R^3$ is $C_{1-6}$alkyl functionalized with halogen.

23. A pharmaceutical composition that provides a therapeutically effective amount of a compound of claim 1 and one or more pharmaceutically acceptable excipients.

24. A pharmaceutical composition that provides a therapeutically effective amount of a compound of claim 1 in combination with at least one further therapeutic agent and one or more pharmaceutically acceptable excipients.

25. An immunogenic composition comprising an antigen or antigen composition and a compound of claim 1.

26. A pharmaceutical composition that provides a therapeutically effective amount of a compound of claim 8 and one or more pharmaceutically acceptable excipients.

27. A pharmaceutical composition that provides a therapeutically effective amount of a compound of claim 10 and one or more pharmaceutically acceptable excipients.

28. A pharmaceutical composition that provides a therapeutically effective amount of a compound of claim 11 and one or more pharmaceutically acceptable excipients.

29. A pharmaceutical composition that provides a therapeutically effective amount of a compound of claim 15 and one or more pharmaceutically acceptable excipients.

30. A pharmaceutical composition that provides a therapeutically effective amount of a compound of claim 16 and one or more pharmaceutically acceptable excipients.

31. A pharmaceutical composition that provides a therapeutically effective amount of a compound of claim 17 and one or more pharmaceutically acceptable excipients.

32. A pharmaceutical composition that provides a therapeutically effective amount of a compound of claim 18 and one or more pharmaceutically acceptable excipients.