methylphenyl]amino]-6-(5-thiazolyl)-1,3,5-triazin-2-yl]-L-Valine;

(42) s-Triazine, 2-phenyl-4,6-bis[[6-[[4-phenyl-6-[[6-[[4-phenyl-6-(trichloromethyl)-s-triazin-2-yl]amino]hexyl]amino]-s-triazin-2-yl]amino]hexyl]amino]-;

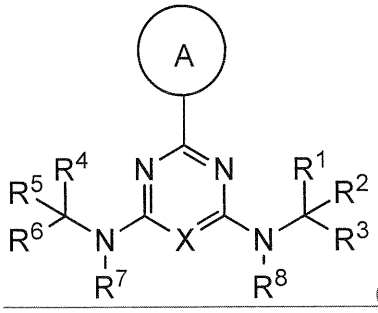
(43) α,α'-[(6-phenyl-1,3,5-triazine-2,4-diyl)bis[imino(1,1,2,2-tetrafluoro-3-oxo-3,1-propanediyl)]]bis[ω-[tetrafluoro(trifluoromethyl)ethoxy]-Poly[oxy[trifluoro(trifluoromethyl)-1,2-ethanediyl]];

(44) α-[[4-[[(3-chlorophenyl)methyl]amino]-6-(1H-imidazol-1-yl)-1,3,5-triazin-2-yl]amino]-N-[[4-(trifluoromethyl)phenyl]methyl]-, (αR)-Cyclohexanepropanamide;

(45) 6-(1H-imidazol-1-yl)-N2,N4-bis(1-methylethyl)-1,3,5-Triazine-2,4-diamine; and

(46) N2,N4-bis(1-methylpropyl)-6-phenyl-1,3,5-Triazine-2,4-diamine.

In an aspect, there is provided a compound having Formula I or a pharmaceutically acceptable salt or hydrate thereof:



(I), wherein:

ring A is an optionally substituted 5-6 member monocyclic aryl or monocyclic heteroaryl;

X is N, CH or C-halo;

R^1, R^3, R^4, and R^6 are each independently selected from hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, -O-C_1-C_4 alkyl, and CN, wherein each said alkyl moiety of R^1, R^3, R^4, and R^6 are each independently optionally substituted with -OH, $-NH_2$, -CN, -O-C_1-C_4 alkyl, -NH(C_1-C_4 alkyl), or -N(C_1-C_4 alkyl)$_2$;

R^2 and R^5 are each independently selected from: -(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-C(O)-NH_2, -(C_1-C_6 alkyl)-CO_2H, -(C_2-C_6 alkenyl or alkynyl), -(C_1-C_6 alkylene)-N(R^6)-(C_1-C_6 alkylene)-O-(C_1-C_6 alkyl), -(C_1-C_6 alkylene)-N(R^6)-(C_0-C_6 alkylene)-Q, -(C_1-C_6 alkylene)-N(R^6)(R^6), -(C_1-C_6 alkylene)-N(R^6)-S(O)$_{1-2}$-(C_1-C_6 alkyl), -(C_1-C_6 alkylene)-N(R^6)-S(O)$_{1-2}$-(C_0-C_6 alkyl)-Q, -(C_1-C_6

alkylene)-S(O)$_{1-2}$-N(R^6)(R^6), -(C$_1$-C$_4$ alkylene)-S(O)$_{1-2}$-N(R^6)-(C$_1$-C$_6$ alkylene)-Q, -C(O)N(R^6)-(C$_1$-C$_6$ alkylene)-C(O)- (C$_0$-C$_6$ alkylene)-O-(C$_1$-C$_6$ alkyl), -C(O)N(R^6)-(C$_1$-C$_6$ alkylene)-C(O)-(C$_0$-C$_6$ alkylene)-O-(C$_0$-C$_6$ alkylene)-Q, -(C$_1$-C$_6$ alkylene)-O-C(O)-(C$_1$-C$_6$ alkyl), -(C$_1$-C$_6$ alkylene)-O-C(O)-(C$_0$-C$_6$ alkyl)-Q, -(C$_1$-C$_6$ alkylene)-O-(C$_1$-C$_6$ alkyl), -(C$_1$-C$_6$ alkylene)-O-(C$_1$-C$_6$ alkylene)-Q, -(C$_0$-C$_6$ alkylene)-C(O)-(C$_0$-C$_6$ alkylene)-O-(C$_1$-C$_6$ alkyl), -(C$_0$-C$_6$ alkylene)-C(O)-(C$_0$-C$_6$ alkylene)-O-(C$_1$-C$_6$ alkylene)-Q, -(C$_1$-C$_6$ alkylene)-O-C(O)-(C$_1$-C$_6$ alkyl), -(C$_1$-C$_6$ alkylene)-O-C(O)-(C$_0$-C$_6$ alkylene)-Q, -(C$_0$-C$_6$ alkylene)-C(O)N(R^6)-(C$_1$-C$_6$ alkyl), -(C$_0$-C$_6$ alkylene)-C(O)N(R^6)-(C$_0$-C$_6$ alkylene)-Q, -(C$_1$-C$_6$ alkylene)-N(R^6)C(O)-(C$_1$-C$_6$ alkyl), -(C$_1$-C$_6$ alkylene)-N(R^6)C(O)-(C$_0$-C$_6$ alkylene)-Q, -(C$_0$-C$_6$ alkylene)-S(O)$_{0-2}$-(C$_1$-C$_6$ alkyl), -(C$_0$-C$_6$ alkylene)-S(O)$_{0-2}$-(C$_0$-C$_6$ alkylene)-Q, -(C$_1$-C$_6$ alkylene)-N(R^6)-C(O)-N(R^6)-(C$_1$-C$_6$ alkyl), -(C$_0$-C$_6$ alkylene)-Q, -(C$_0$-C$_6$ alkylene)-C(O)-(C$_1$-C$_6$ alkyl), -(C$_0$-C$_6$ alkylene)-C(O)-(C$_0$-C$_6$ alkylene)-Q, wherein:

any alkyl or alkylene moiety present in R^2 and R^5 is optionally substituted with one or more -OH, -O(C$_1$-C$_4$ alkyl), -CO$_2$H, or halo;

any terminal methyl moiety present in R^2 and R^5 is optionally replaced with -CH$_2$OH, CF$_3$, -CH$_2$F, -CH$_2$Cl, C(O)CH$_3$, C(O)CF$_3$, CN, or CO$_2$H;

R^7 and R^8 are each independently selected from hydrogen and C$_1$-C$_6$ alkyl; and

Q is selected from aryl, heteroaryl, carbocyclyl and heterocyclyl, any of which is optionally substituted; wherein

R^1 and R^3 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

R^4 and R^6 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

R^1 and R^2 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl; or

R^4 and R^5 are optionally taken together to form an optionally substituted carbocyclyl, optionally substituted heterocyclyl, an optionally substituted aryl, or an optionally substituted heteroaryl; wherein:

(i) when X is N and A is optionally substituted phenyl, then (a) neither N(R^7)C(R^4)(R^5)(R^6) nor N(R^8)C(R^1)(R^2)(R^3) is NHCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$NH$_2$, 4-[[2-[2-

(2-aminoethoxy)ethoxy]ethyl]amino] and (b) $N(R^7)C(R^4)(R^5)(R^6)$ and $N(R^8)C(R^1)(R^2)(R^3)$ are not both NHEt, NH(n-propyl), NH(n-butyl), NH(n-docecyl), NH-[(4- methoxyphenyl)methyl], $NHCH_2CH_2CHO$, $NHCH_2CH_2OCH_3$, $NHCH_2CH_2OH$, $NHCH_2CH(OH)CH_3$, $NHCH_2CH_2OC(O)$phenyl, $NHCH_2CH_2CH_2OH$, $NHCH_2CH_2CH_2N(CH_3)$phenyl, $NHCH_2C(O)OCH_3$, $NHCH_2C(O)OCH_2CH_3$, $NHCH_2$phenyl, $NHCH(CH_3)CH_2CH_3$, or $NHCH_2CH_2OC(O)CH_3$;

(ii) when X is CH or C-Cl and A is phenyl optionally substituted with F, Cl or SO_2CH_3, then neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is $N(CH_3)CH_2C(O)$NH-i-propyl, $NHCH(CH_3)(CH_2)_3N(CH_2CH_3)_2$, $NHCH_2CH_2OH$, $NHCH_2CH_2OCH_3$, $NHCH_2CH_2OSO_3H$, $NHCH_2CH_2CH_2OCH_2CH_2O$-phenyl, $NHCH_2CH_2CH_2OH$, $NHCH_2CH_2CH_2OCH_3$, $NHCH_2CH(OH)CH_3$, $N(CH_2CH_3)_2$, NH-i-propyl, $NHCH_2CH_2NHC(O)OCH_3$, $NHCH_2CH_2NHC(O)CH_3$, $NHCH_2CH_2NH_2$, or $NHCH_2$-phenyl;

(iii) when X is CH and A is optionally substituted pyridyl, then neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is $NHCH_2$-phenyl, $NHCH_2$-(2,4-difluorophenyl), $N(CH_3)CH_2CH_2C(O)OH$, $NHCH_2CH_2C(O)OH$, $NHCH_2CH_2C(O)OCH_2CH_3$, $NHCH_2CH_2C(O)O$-t-butyl, $NHCH_2CH_2C(O)NH_2$, $NHCH_2CH_2$-phenyl, $NHCH_2CH_2OH$, $NHCH_2CH_2NH_2$, $NHCH_2CH_2N(CH_3)_2$, or $NHCH_2CH_2CH_3$;

(iv) when X is CH and A is optionally substituted 1-imidazolyl, optionally substituted 1-pyrrolyl or optionally substituted 1-pyrazolyl, then neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is $NH(CH_2)_7CH_3$, $NHCH_2$-(o-chloro-phenyl), or $NHCH_2CH_2OH$;

(v) when X is N and A is an optionally substituted pyridyl, then (A) neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is NHC(O)-[2-chloro-4-(methylsulfonyl)], $N(CH_3)_2$, $NHCH_2CH_2CH_2SO_2CH_2CH_2Cl$, $NHCH_2CH_2OCH_2CH_2SO_2CH_2CH_2Cl$,or $NHCH_2CH_2SO_2CH_2CH_2Cl$, (B) $N(R^7)C(R^4)(R^5)(R^6)$ and $N(R^8)C(R^1)(R^2)(R^3)$ are not both $NHC(O)C(CH_3)_3$, $NHC(O)CH=CH_2$, $NHC(O)C(CH_3)=CH_2$, $NHCH_2CH_2OH$, NH-cyclohexyl, $NHCH_2$-phenyl, NHC(O)phenyl, $NHC(O)(CH_2)_5NH_2$, $NHC(O)OCH_3$, $NHC(O)CH_3$, and NHC(O)NH-optionally substituted phenyl, and (C) when $N(R^7)C(R^4)(R^5)(R^6)$ is $NHC(CH_3)_3$, then $N(R^8)C(R^1)(R^2)(R^3)$ is not $NHCH_2$-phenyl or $NH\text{-}CH_2CH_3$;

(vi) when X is N and A is an optionally substituted heteroaryl, then $N(R^7)C(R^4)(R^5)(R^6)$ and $N(R^8)C(R^1)(R^2)(R^3)$ are not both $N(CH_2CH_3)_2$, $NHCH_2CH_2$-i-propyl, $NHCH_2CH(CH_3)_2$, and $NHC(O)CH_3$;

(vii) when X is CH and A is unsubstituted 2-pyridinyl, then the ring formed by R^4 and R^5 is not 5-methyl-1H-pyrazol-3-yl,

(viii) when A is optionally substituted 1-pyrazolyl, then neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is $N(CH_3)_2$, $NHCH_3$, NHAc, NHisopropyl, $NHCH_2CH_3$, $NHCH_2CH_2SO_3H$ or $N(CH_2CH_3)_2$,

(ix) when X is N and A is optionally substituted phenyl, thienyl, or pyridinyl, then neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is NHcyclohexylC(O)$NHCH_2$R, wherein R is phenyl or pyridinyl which is substituted with one or more of OCF_3, OCH_3, chloro, or CF_3,

(x) when X is N, A is an optionally substituted phenyl and R^4 and R^5 form an optionally substituted phenyl, then $N(R^8)C(R^1)(R^2)(R^3)$ is not $NHCH_2$(4-fluorophenyl), $NHCH_2CO_2H$, $NHCH_2C(O)Cl$, $NHCH(CO_2H)(CH_2SCH_2$phenyl), or $NHCH_2C(O)NHC(O)NHR$ or $NHCH_2C(O)NHC(S)NHR$, wherein R is optionally substituted phenyl or naphthyl,

(xi) when X is N, A is an oxadiazole substituted with an optionally substituted pyridinyl, then R^4 and R^5 do not form an optionally substituted phenyl,

(xii) when A is substituted 1-pyrazolyl, then (A) then $N(R^7)C(R^4)(R^5)(R^6)$ and $N(R^8)C(R^1)(R^2)(R^3)$ are not both $NHC(CH_3)_3$, and (B) A is not substituted with N=N-R, wherein R is a ring,

(xiii) the compound is not selected from the group:

(1) N-(2-aminophenyl)-4-[[[4-[(2,3-dihydro-1H-inden-2-yl)amino]-6-phenyl-1,3,5-triazin-2-yl]amino]methyl]-benzamide,

(2) 2-chloro-N-[4-(cyclopropylamino)-6-(2-pyridinyl)-1,3,5-triazin-2-yl]-4-(methylsulfonyl)-benzamide,

(3) 2-[[1-[4-(cyclopropylamino)-6-(ethylamino)-1,3,5-triazin-2-yl]-1H-1,2,4-triazol-3-yl]thio]-acetamide,

(4) N^2-cyclopropyl-N^4-ethyl-6-[3-[(phenylmethyl)thio]-1H-1,2,4-triazol-1-yl]-1,3,5-triazine-2,4-diamine,

(5) 2-[[1-[4-(cyclopropylamino)-6-(ethylamino)-1,3,5-triazin-2-yl]-1H-1,2,4-triazol-3-yl]thio]-

acetic acid methyl ester,

(6) N-[[4-[[[4-(cyclopropylamino)-6-(2-pyridinyl)-1,3,5-triazin-2-yl]amino]methyl]cyclohexyl] methyl]-4-fluoro-benzenesulfonamide,

(7) N^2-cyclopropyl-6-(3,5-dimethyl-1H-pyrazol-1-yl)-N^4-phenyl-1,3,5-triazine-2,4-diamine,

(8) N^2,N^4-dicyclohexyl-6-[3-(4-methoxyphenyl)-5-(methylthio)-1H-pyrazol-1-yl]-1,3,5-triazine-2,4-diamine,

(9) N^2,N^4-dicyclohexyl-6-[3-(3,4-dimethoxyphenyl)-5-(methylthio)-1H-pyrazol-1-yl]-1,3,5-triazine-2,4-diamine,

(10) N^2,N^4-dicyclohexyl-6-[5-(methylthio)-3-(3,4,5-trimethoxyphenyl)-1H-pyrazol-1-yl]-1,3,5-triazine-2,4-diamine,

(11) N^2,N^4-dicyclohexyl-6-phenyl-1,3,5-triazine-2,4-diamine,

(12) 1,1'-[(6-phenyl-s-triazine-2,4-diyl)diimino]bis[dodecahydro-anthraquinone],

(13) 4,4'-[(6-phenyl-1,3,5-triazine-2,4- diyl)bis(iminomethylene)]bis[2,6-bis(1,1- dimethylethyl)-phenol,

(14) N-[4-[(4-aminobutyl)amino]-6-[5-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl] amino]-2-methylphenyl]-1,3,5-triazin-2-yl]-glycine,

(15) 4-[2-[[4-[(5-aminopentyl)amino]-6-(3- fluorophenyl)-1,3,5-triazin-2-yl]amino]ethyl]-phenol,

(16) 4-[2-[[4-[(5-aminopentyl)amino]-6-(4- fluorophenyl)-1,3,5-triazin-2-yl]amino]ethyl]-phenol,

(17) 6-(4-aminopyridin-3-yl)-N^2-benzyl-N^4-(tert-butyl)-1,3,5-triazine-2,4-diamine,

(18) N^2,N^4-bis(cyclohexylmethyl)-6-phenyl-1,3,5-triazine-2,4-diamine,

(19) 4,4'-[[6-[3,5-bis(1,1-dimethylethyl)-4- hydroxyphenyl]-1,3,5-triazine-2,4-diyl]bis(imino-3,1-propanediyl)]bis[2,6-bis(1,1-dimethylethyl)-phenol,

(20) 4,4'-[(6-phenyl-1,3,5-triazine-2,4- diyl)bis(imino-3,1-propanediyl)]bis[2,6-bis(1,1-dimethylethyl)-phenol,

(21) N-[6-[(2,3-dihydro-1H-inden-2-yl)amino]-2-(2-pyridinyl)-4-pyrimidinyl]-β alanine,

(22) N^4-cyclopentyl-2-phenyl-N^6-(phenylmethyl)-4,6-pyrimidinediamine,

(23) 2-[[6-(bicyclo[2.2.1]hept-2-ylamino)-2-phenyl-4-pyrimidinyl]amino]-ethanol,

(24) N^2-isopropyl-6-phenyl-N4-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazine-2,4-diamine,

(25) 2-chloro-4-(methylsulfonyl)-*N*-[4-[(phenylmethyl)amino]-6-(2-pyridinyl)-1,3,5-triazin-2-yl]-benzamide,

(26) *N*-[[4-[[[4-(cyclopropylamino)-6-(2-pyridinyl)-1,3,5-triazin-2-yl]amino]methyl]cyclohexyl]methyl]-4-fluoro-benzenesulfonamide,

(27) [[4-[[[[[4-amino-6-(4-pyridinyl)-1,3,5-triazin-2-yl]amino]methoxy]methyl]amino]-6-(4-pyridinyl)-1,3,5-triazin-2-yl]imino]bis-methanol,

(28) [[4-[[[[[4-[bis(hydroxymethyl)amino]-6-(4-pyridinyl)-1,3,5-triazin-2-yl]amino]methoxy]methyl](hydroxymethyl)amino]-6-(4-pyridinyl)-1,3,5-triazin-2-yl]imino]bis-methanol,

(29) 5-[4,6-bis(diethylamino)-1,3,5-triazin-2-yl]- 2*H*-tetrazole-2-acetic acid ethyl ester,

(30) N^2,N^2,N^4,N^4-tetraethyl-6-(2*H*-tetrazol-5-yl)-1,3,5-triazine-2,4-diamine,

(31) *N*,*N*'-[6-[4-(acetylamino)-1,2,5-oxadiazol-3-yl]-1,3,5-triazine-2,4-diyl]bis-acetamide,

(32) N-(2-chloro-6-methylphenyl)-5-[[4-(dimethylamino)-6-(2-pyridinyl)-1,3,5-triazin-2-yl]amino]-1,3,4-Oxadiazole-2-carboxamide,

(33) N4-(5-methyl-1H-pyrazol-3-yl)-2-(2-pyridinyl)-N6-(tetrahydro-2H-pyran-4-yl)-4,6-Pyrimidinediamine,

(34) 6-(4-chlorophenyl)-N2-[4-chloro-3-(trifluoromethyl)phenyl]-N4-[3-(diethylamino)propyl]-1,3,5-Triazine-2,4-diamine,

(35) 6-(4-chlorophenyl)-N2-[4-chloro-3-(trifluoromethyl)phenyl]-N4-[3-(dimethylamino)propyl]- 1,3,5-Triazine-2,4-diamine,

(36) N2-[3,5-bis(trifluoromethyl)phenyl]-6-(4-chlorophenyl)-N4-[3-(diethylamino)propyl]-1,3,5-Triazine-2,4-diamine,

(37) N2,N4-bis[(4-methoxyphenyl)methyl]-6-[4-(trifluoromethoxy)phenyl]-1,3,5-Triazine-2,4-diamine,

(38) N,N''-(6-phenyl-1,3,5-triazine-2,4-diyl)bis[N'-(2-chloroethyl)-Urea,

(39) N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-methyl-3-[[4-phenyl-6-(propylamino)-1,3,5-triazin-2-yl]amino]phenyl]-urea,

(40) N-[4-[[5-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenyl]amino]-6-(4-pyridinyl)-1,3,5-triazin-2-yl]-glycine,

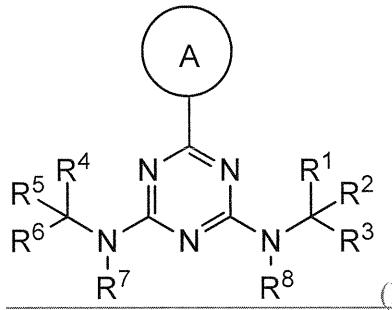
(41) N-[4-[[5-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenyl]amino]-6-(5-thiazolyl)-1,3,5-triazin-2-yl]-L-Valine,

(42) s-Triazine, 2-phenyl-4,6-bis[[6-[[4-phenyl-6-[[6-[[4-phenyl-6-(trichloromethyl)-s-triazin-2-yl]amino]hexyl]amino]-s-triazin-2-yl]amino]hexyl]amino]-,

(43) α,α'-[(6-phenyl-1,3,5-triazine-2,4-diyl)bis[imino(1,1,2,2-tetrafluoro-3-oxo-3,1-propanediyl)]]bis[ω-[tetrafluoro(trifluoromethyl)ethoxy]-Poly[oxy[trifluoro(trifluoromethyl)-1,2-ethanediyl]], and

(44) α-[[4-[[(3-chlorophenyl)methyl]amino]-6-(1H-imidazol-1-yl)-1,3,5-triazin-2-yl]amino]-N-[[4-(trifluoromethyl)phenyl]methyl]-, (αR)-Cyclohexanepropanamide.

In another aspect, there is provided a compound having Formula Ia or a pharmaceutically acceptable salt or hydrate thereof:



(Ia), wherein:

ring A is an optionally substituted 5-6 member monocyclic aryl or monocyclic heteroaryl;

R^1, R^3, R^4, and R^6 are each independently selected from hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, -O-C_1-C_4 alkyl, and CN, wherein each said alkyl moiety of R^1, R^3, R^4, and R^6 are each independently optionally substituted with -OH, $-NH_2$, -CN, -O-C_1-C_4 alkyl, -NH(C_1-C_4 alkyl), or -N(C_1-C_4 alkyl)$_2$;

R^2 and R^5 are each independently selected from: -(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-C(O)-NH_2, -(C_1-C_6 alkyl)-CO_2H, -(C_2-C_6 alkenyl or alkynyl), -(C_1-C_6 alkylene)-N(R^6)-(C_1-C_6 alkylene)-O-(C_1-C_6 alkyl), -(C_1-C_6 alkylene)-N(R^6)-(C_0-C_6 alkylene)-Q, -(C_1-C_6 alkylene)-N(R^6)(R^6), -(C_1-C_6 alkylene)-N(R^6)-S(O)$_{1-2}$-(C_1-C_6 alkyl), -(C_1-C_6 alkylene)-N(R^6)-S(O)$_{1-2}$-(C_0-C_6 alkyl)-Q, -(C_1-C_6 alkylene)-S(O)$_{1-2}$-N(R^6)(R^6), -(C_1-C_4

alkylene)-$S(O)_{1-2}$-$N(R^6)$-(C_1-C_6 alkylene)-Q, -$C(O)N(R^6)$-(C_1-C_6 alkylene)-C(O)- (C_0-C_6 alkylene)-O-(C_1-C_6 alkyl), -$C(O)N(R^6)$-(C_1-C_6 alkylene)-C(O)-(C_0-C_6 alkylene)-O-(C_0-C_6 alkylene)-Q, -(C_1-C_6 alkylene)-O-C(O)-(C_1-C_6 alkyl), -(C_1-C_6 alkylene)-O-C(O)-(C_0-C_6 alkyl)-Q, -(C_1-C_6 alkylene)-O-(C_1-C_6 alkyl), -(C_1-C_6 alkylene)-O-(C_1-C_6 alkylene)-Q, -(C_0-C_6 alkylene)-C(O)-(C_0-C_6 alkylene)-O-(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-C(O)-(C_0-C_6 alkylene)-O-(C_1-C_6 alkylene)-Q, -(C_1-C_6 alkylene)-O-C(O)-(C_1-C_6 alkyl), -(C_1-C_6 alkylene)-O-C(O)-(C_0-C_6 alkylene)-Q, -(C_0-C_6 alkylene)-$C(O)N(R^6)$-(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-$C(O)N(R^6)$-(C_0-C_6 alkylene)-Q, -(C_1-C_6 alkylene)-$N(R^6)C(O)$-(C_1-C_6 alkyl), -(C_1-C_6 alkylene)-$N(R^6)C(O)$-(C_0-C_6 alkylene)-Q, -(C_0-C_6 alkylene)-$S(O)_{0-2}$-(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-$S(O)_{0-2}$-(C_0-C_6 alkylene)-Q, -(C_1-C_6 alkylene)-$N(R^6)$-C(O)-$N(R^6)$-(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-Q, -(C_0-C_6 alkylene)-C(O)-(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-C(O)-(C_0-C_6 alkylene)-Q, wherein:

any alkyl or alkylene moiety present in R^2 and R^5 is optionally substituted with one or more -OH, -O(C_1-C_4 alkyl), -CO_2H, or halo;

any terminal methyl moiety present in R^2 and R^5 is optionally replaced with -CH_2OH, CF_3, -CH_2F, -CH_2Cl, $C(O)CH_3$, $C(O)CF_3$, CN, or CO_2H;

R^7 and R^8 are each independently selected from hydrogen and C_1-C_6 alkyl; and

Q is selected from aryl, heteroaryl, carbocyclyl and heterocyclyl, any of which is optionally substituted; wherein

R^1 and R^3 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

R^4 and R^6 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

R^1 and R^2 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl; or

R^4 and R^5 are optionally taken together to form an optionally substituted carbocyclyl, optionally substituted heterocyclyl, an optionally substituted aryl, or an optionally substituted heteroaryl;

wherein:

(i) when A is optionally substituted phenyl, then (a) neither $N(R^7)C(R^4)(R^5)(R^6)$ nor

$N(R^8)C(R^1)(R^2)(R^3)$ is $NHCH_2CH_2OCH_2CH_2OCH_2CH_2NH_2$ or 4-[[2-[2-(2-aminoethoxy)ethoxy]ethyl]amino] and (b) $N(R^7)C(R^4)(R^5)(R^6)$ and $N(R^8)C(R^1)(R^2)(R^3)$ are not both NHEt, NH(n-propyl), NH(n-butyl), NH(n-dococyl), NH-[(4- methoxyphenyl)methyl], $NHCH_2CH_2CHO$, $NHCH_2CH_2OCH_3$, $NHCH_2CH_2OH$, $NHCH_2CH(OH)CH_3$, $NHCH_2CH_2OC(O)$phenyl, $NHCH_2CH_2CH_2OH$, $NHCH_2CH_2CH_2N(CH_3)$phenyl, $NHCH_2C(O)OCH_3$, $NHCH_2C(O)OCH_2CH_3$, $NHCH_2$phenyl, $NHCH(CH_3)CH_2CH_3$, or $NHCH_2CH_2OC(O)CH_3$;

(ii) when A is an optionally substituted pyridyl, then (A) neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is NHC(O)-[2-chloro-4-(methylsulfonyl)], $N(CH_3)_2$, $NHCH_2CH_2CH_2SO_2CH_2CH_2Cl$, $NHCH_2CH_2OCH_2CH_2SO_2CH_2CH_2Cl$,or $NHCH_2CH_2SO_2CH_2CH_2Cl$, (B) $N(R^7)C(R^4)(R^5)(R^6)$ and $N(R^8)C(R^1)(R^2)(R^3)$ are not both $NHC(O)C(CH_3)_3$, $NHC(O)CH=CH_2$, $NHC(O)C(CH_3)=CH_2$, $NHCH_2CH_2OH$, NH-cyclohexyl, $NHCH_2$-phenyl, NHC(O)phenyl, $NHC(O)(CH_2)_5NH_2$, $NHC(O)OCH_3$, $NHC(O)CH_3$, and NHC(O)NH-optionally substituted phenyl, and (C) when $N(R^7)C(R^4)(R^5)(R^6)$ is $NHC(CH_3)_3$, then $N(R^8)C(R^1)(R^2)(R^3)$ is not $NHCH_2$-phenyl or $NH\text{-}CH_2CH_3$;

(iii) when A is an optionally substituted heteroaryl, then $N(R^7)C(R^4)(R^5)(R^6)$ and $N(R^8)C(R^1)(R^2)(R^3)$ are not both $N(CH_2CH_3)_2$, $NHCH_2CH_2$-i-propyl, $NHCH_2CH(CH_3)_2$, and $NHC(O)CH_3$;

(iv) when A is optionally substituted 1-pyrazolyl, then neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is $N(CH_3)_2$, $NHCH_3$, NHAc, NHisopropyl, $NHCH_2CH_3$, $NHCH_2CH_2SO_3H$ or $N(CH_2CH_3)_2$,

(v) when A is optionally substituted phenyl, thienyl, or pyridinyl, then neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is NHcyclohexylC(O)$NHCH_2R$, wherein R is phenyl or pyridinyl which is substituted with one or more of OCF_3, OCH_3, chloro, or CF_3,

(vi) when A is an optionally substituted phenyl and R^4 and R^5 form an optionally substituted phenyl, then $N(R^8)C(R^1)(R^2)(R^3)$ is not $NHCH_2$(4-fluorophenyl), $NHCH_2CO_2H$, $NHCH_2C(O)Cl$, $NHCH(CO_2H)(CH_2SCH_2$phenyl), or $NHCH_2C(O)NHC(O)NHR$ or $NHCH_2C(O)NHC(S)NHR$, wherein R is optionally substituted phenyl or naphthyl,

(vii) when A is an oxadiazole substituted with an optionally substituted pyridinyl, then R^4 and R^5 do not form an optionally substituted phenyl,

(viii) when A is substituted 1-pyrazolyl, then (A) then $N(R^7)C(R^4)(R^5)(R^6)$ and $N(R^8)C(R^1)(R^2)(R^3)$ are not both $NHC(CH_3)_3$, and (B) A is not substituted with N=N-R, wherein R is a ring,

(ix) the compound is not selected from the group:

(1) N-(2-aminophenyl)-4-[[[4-[(2,3-dihydro-1H-inden-2-yl)amino]-6-phenyl-1,3,5-triazin-2-yl]amino]methyl]-benzamide,

(2) 2-chloro-N-[4-(cyclopropylamino)-6-(2-pyridinyl)-1,3,5-triazin-2-yl]-4-(methylsulfonyl)-benzamide,

(3) 2-[[1-[4-(cyclopropylamino)-6-(ethylamino)-1,3,5-triazin-2-yl]-1H-1,2,4-triazol-3-yl]thio]-acetamide,

(4) N^2-cyclopropyl-N^4-ethyl-6-[3-[(phenylmethyl)thio]-1H-1,2,4-triazol-1-yl]-1,3,5-triazine-2,4-diamine,

(5) 2-[[1-[4-(cyclopropylamino)-6-(ethylamino)-1,3,5-triazin-2-yl]-1H-1,2,4-triazol-3-yl]thio]-acetic acid methyl ester,

(6) N-[[4-[[[4-(cyclopropylamino)-6-(2-pyridinyl)-1,3,5-triazin-2-yl]amino]methyl]cyclohexyl]methyl]-4-fluoro-benzenesulfonamide,

(7) N^2-cyclopropyl-6-(3,5-dimethyl-1H-pyrazol-1-yl)-N^4-phenyl-1,3,5-triazine-2,4-diamine,

(8) N^2,N^4-dicyclohexyl-6-[3-(4-methoxyphenyl)-5-(methylthio)-1H-pyrazol-1-yl]-1,3,5-triazine-2,4-diamine,

(9) N^2,N^4-dicyclohexyl-6-[3-(3,4-dimethoxyphenyl)-5-(methylthio)-1H-pyrazol-1-yl]-1,3,5-triazine-2,4-diamine,

(10) N^2,N^4-dicyclohexyl-6-[5-(methylthio)-3-(3,4,5-trimethoxyphenyl)-1H-pyrazol-1-yl]-1,3,5-triazine-2,4-diamine,

(11) N^2,N^4-dicyclohexyl-6-phenyl-1,3,5-triazine-2,4-diamine,

(12) 1,1'-[(6-phenyl-s-triazine-2,4-diyl)diimino]bis[dodecahydro-anthraquinone],

(13) 4,4'-[(6-phenyl-1,3,5-triazine-2,4- diyl)bis(iminomethylene)]bis[2,6-bis(1,1- dimethylethyl)-phenol,

(14) N-[4-[(4-aminobutyl)amino]-6-[5-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenyl]-1,3,5-triazin-2-yl]-glycine,

(15) 4-[2-[[4-[(5-aminopentyl)amino]-6-(3-fluorophenyl)-1,3,5-triazin-2-yl]amino]ethyl]-phenol,

(16) 4-[2-[[4-[(5-aminopentyl)amino]-6-(4-fluorophenyl)-1,3,5-triazin-2-yl]amino]ethyl]-phenol,

(17) 6-(4-aminopyridin-3-yl)-N^2-benzyl-N^4-(tert-butyl)-1,3,5-triazine-2,4-diamine,

(18) N^2,N^4-bis(cyclohexylmethyl)-6-phenyl-1,3,5-triazine-2,4-diamine,

(19) 4,4'-[[6-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-1,3,5-triazine-2,4-diyl]bis(imino-3,1-propanediyl)]bis[2,6-bis(1,1-dimethylethyl)-phenol,

(20) 4,4'-[(6-phenyl-1,3,5-triazine-2,4-diyl)bis(imino-3,1-propanediyl)]bis[2,6-bis(1,1-dimethylethyl)-phenol,

(21) N^2-isopropyl-6-phenyl-N4-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazine-2,4-diamine,

(22) 2-chloro-4-(methylsulfonyl)-*N*-[4-[(phenylmethyl)amino]-6-(2-pyridinyl)-1,3,5-triazin-2-yl]-benzamide,

(23) *N*-[[4-[[[4-(cyclopropylamino)-6-(2-pyridinyl)-1,3,5-triazin-2-yl]amino]methyl]cyclohexyl]methyl]-4-fluoro-benzenesulfonamide,

(24) [[4-[[[[[4-amino-6-(4-pyridinyl)-1,3,5-triazin-2-yl]amino]methoxy]methyl]amino]-6-(4-pyridinyl)-1,3,5-triazin-2-yl]imino]bis-methanol,

(25) [[4-[[[[[4-[bis(hydroxymethyl)amino]-6-(4-pyridinyl)-1,3,5-triazin-2-yl]amino]methoxy]methyl](hydroxymethyl)amino]-6-(4-pyridinyl)-1,3,5-triazin-2-yl]imino]bis-methanol,

(26) 5-[4,6-bis(diethylamino)-1,3,5-triazin-2-yl]- 2*H*-tetrazole-2-acetic acid ethyl ester,

(27) N^2,N^2,N^4,N^4-tetraethyl-6-(2*H*-tetrazol-5-yl)-1,3,5-triazine-2,4-diamine,

(28) *N*,*N*'-[6-[4-(acetylamino)-1,2,5-oxadiazol-3-yl]-1,3,5-triazine-2,4-diyl]bis-acetamide,

(29) N-(2-chloro-6-methylphenyl)-5-[[4-(dimethylamino)-6-(2-pyridinyl)-1,3,5-triazin-2-yl]amino]-1,3,4-Oxadiazole-2-carboxamide,

(30) 6-(4-chlorophenyl)-N2-[4-chloro-3-(trifluoromethyl)phenyl]-N4-[3-(diethylamino)propyl]-1,3,5-Triazine-2,4-diamine,

(31) 6-(4-chlorophenyl)-N2-[4-chloro-3-(trifluoromethyl)phenyl]-N4-[3-(dimethylamino)propyl]- 1,3,5-Triazine-2,4-diamine,

(32) N2-[3,5-bis(trifluoromethyl)phenyl]-6-(4-chlorophenyl)-N4-[3-(diethylamino)propyl]-1,3,5-Triazine-2,4-diamine,

(33) N2,N4-bis[(4-methoxyphenyl)methyl]-6-[4-(trifluoromethoxy)phenyl]-1,3,5-Triazine-2,4-diamine,

(34) N,N''-(6-phenyl-1,3,5-triazine-2,4-diyl)bis[N'-(2-chloroethyl)-Urea,

(35) N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-methyl-3-[[4-phenyl-6-(propylamino)-1,3,5-triazin-2-yl]amino]phenyl]-urea,

(36) N-[4-[[5-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenyl]amino]-6-(4-pyridinyl)-1,3,5-triazin-2-yl]-glycine,

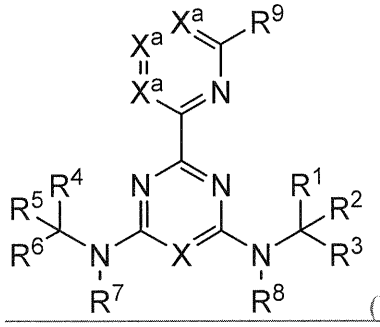
(37) N-[4-[[5-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenyl]amino]-6-(5-thiazolyl)-1,3,5-triazin-2-yl]-L-Valine,

(38) s-Triazine, 2-phenyl-4,6-bis[[6-[[4-phenyl-6-[[6-[[4-phenyl-6-(trichloromethyl)-s-triazin-2-yl]amino]hexyl]amino]-s-triazin-2-yl]amino]hexyl]amino]-,

(39) α,α'-[(6-phenyl-1,3,5-triazine-2,4-diyl)bis[imino(1,1,2,2-tetrafluoro-3-oxo-3,1-propanediyl)]]bis[ω-[tetrafluoro(trifluoromethyl)ethoxy]-Poly[oxy[trifluoro(trifluoromethyl)-1,2-ethanediyl]], and

(40) α-[[4-[[(3-chlorophenyl)methyl]amino]-6-(1H-imidazol-1-yl)-1,3,5-triazin-2-yl]amino]-N-[[4-(trifluoromethyl)phenyl]methyl]-, (αR)-Cyclohexanepropanamide.

In yet another aspect, there is provided a compound having Formula B, or pharmaceutically acceptable salt or hydrate thereof:



(B), wherein:

X is N, CH or C-halo;

X^a is N or C-R^{9a}, provided that when one X^a is N, then the other two X^a are both C-R^{9a};

R^9 is halo, -C_1-C_4 alkyl, -C_1-C_4 haloalkyl, -C_1-C_4 hydroxyalkyl, -NH-$S(O)_2$-(C_1-C_4 alkyl), -$S(O)_2$NH(C_1-C_4 alkyl), -CN, -$S(O)_2$-(C_1-C_4 alkyl), C_1-C_4 alkoxy, -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)$_2$, -OH, -OCF_3, -CN, -NH_2, -C(O)NH_2, -C(O)NH(C_1-C_4 alkyl), -C(O)-N(C_1-C_4 alkyl)$_2$, -(C_1-C_6 alkylene)-O-(C_1-C_6 alkyl), aryl, and cyclopropyl optionally substituted with OH;

each R^{9a} is independently selected from hydrogen, halo, -C_1-C_4 alkyl, -C_1-C_4 haloalkyl, -C_1-C_4 hydroxyalkyl, -NH-$S(O)_2$-(C_1-C_4 alkyl), -$S(O)_2$NH(C_1-C_4 alkyl), -CN, -$S(O)_2$-(C_1-C_4 alkyl), C_1-C_4 alkoxy, -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)$_2$, -OH, -OCF_3, -CN, -NH_2, -C(O)NH_2, -C(O)NH(C_1-C_4 alkyl), -C(O)-N(C_1-C_4 alkyl)$_2$, -(C_1-C_6 alkylene)-O-(C_1-C_6 alkyl), aryl, and cyclopropyl optionally substituted with OH;

R^1, R^3, R^4, and R^6 are each independently selected from hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, -O-C_1-C_4 alkyl, and CN, wherein each said alkyl moiety of R^1, R^3, R^4, and R^6 are each independently optionally substituted with -OH, -NH_2, -CN, -O-C_1-C_4 alkyl, -NH(C_1-C_4 alkyl), or -N(C_1-C_4 alkyl)$_2$;

R^2 and R^5 are each independently selected from: -(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-C(O)-NH_2, -(C_1-C_6 alkyl)-CO_2H, -(C_2-C_6 alkenyl or alkynyl), -(C_1-C_6 alkylene)-O-(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-C(O)N(R^6)-(C_1-C_6 alkyl)

-(C_0-C_6 alkylene)-Q, -(C_0-C_6 alkylene)-C(O)-(C_1-C_6 alkyl), and -(C_0-C_6 alkylene)-C(O)-(C_0-C_6 alkylene)-Q, wherein:

any alkyl or alkylene moiety present in R^2 and R^5 is optionally substituted with one or more -OH, -O(C_1-C_4 alkyl), -CO_2H, or halo;

any terminal methyl moiety present in R^2 and R^5 is optionally replaced with -CH_2OH, CF_3, -CH_2F, -CH_2Cl, C(O)CH_3, C(O)CF_3, CN, or CO_2H;

R^7 and R^8 are each independently selected from hydrogen and C_1-C_6 alkyl; and

Q is selected from aryl, heteroaryl, carbocyclyl and heterocyclyl, any of which is optionally substituted; wherein

R^1 and R^3 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

R^4 and R^6 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

R^1 and R^2 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl; or

R^4 and R^5 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl, an optionally substituted 5-6 member monocyclic aryl, or an optionally substituted 5-6 member monocyclic heteroaryl;

wherein the compound is not selected from the group:

(1) 4,6-Pyrimidinediamine, 2-(6-methyl-2-pyridinyl)-N4,N6-dipropyl-;

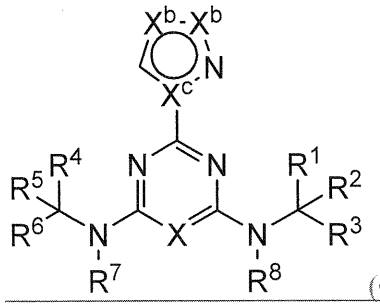
(2) 4,6-Pyrimidinediamine, N4-ethyl-2-(6-methyl-2-pyridinyl)-N6-propyl-;

(3) 4,6-Pyrimidinediamine, N4,N4-diethyl-2-(6-methyl-2-pyridinyl)-N6-propyl-;

(4) [2,4'-Bipyrimidine]-2',4,6-triamine, N6-[2-(dimethylamino)ethyl]-N2',N2',N4,N4-tetramethyl-; or

(5) [2,4'-Bipyrimidine]-2',4,6-triamine, N6-[2-(dimethylamino)ethyl]-N2',N2',N4,N4-tetramethyl-, phosphate.

In yet another aspect, there is provided a compound having Formula C, or pharmaceutically acceptable salt or hydrate thereof:



(C), wherein:

X is N, CH or C-halo;

each X^b is independently N-R^{9b}, O, S, C-H, or C-R^{9c}, provided that at least one X^b is C-R^{9c}, and when one X^b is C-H or C-R^{9c} and the other is C-R^{9c} then X^c is N, and when one X^b is N-R^{9b}, O, or S,then X^c is C;

R^{9b} is hydrogen or -C_1-C_4 alkyl;

R^{9c} is halo, -C_1-C_4 alkyl, -C_1-C_4 haloalkyl, -C_1-C_4 hydroxyalkyl, -NH-$S(O)_2$-(C_1-C_4 alkyl), -$S(O)_2$NH(C_1-C_4 alkyl), -CN, -$S(O)_2$-(C_1-C_4 alkyl), C_1-C_4 alkoxy, -NH(C_1-C_4 alkyl),

-N(C_1-C_4 alkyl)$_2$, -OH, -OCF_3, -CN, -NH_2, -C(O)NH_2, -C(O)NH(C_1-C_4 alkyl), -C(O)-N(C_1-C_4 alkyl)$_2$, -(C_1-C_6 alkylene)-O-(C_1-C_6 alkyl), aryl, and cyclopropyl optionally substituted with OH;

R^1, R^3, R^4, and R^6 are each independently selected from hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, -O-C_1-C_4 alkyl, and CN, wherein each said alkyl moiety of R^1, R^3, R^4, and R^6 are each independently optionally substituted with -OH, -NH_2, -CN, -O-C_1-C_4 alkyl, -NH(C_1-C_4 alkyl), or -N(C_1-C_4 alkyl)$_2$;

R^2 and R^5 are each independently selected from: -(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-C(O)-NH_2, -(C_1-C_6 alkyl)-CO_2H, -(C_0-C_6 alkylene)-Q, -(C_0-C_6 alkylene)-C(O)-(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-C(O)-(C_0-C_6 alkylene)-Q, wherein:

any alkyl or alkylene moiety present in R^2 and R^5 is optionally substituted with one or more -OH, -O(C_1-C_4 alkyl), -CO_2H, or halo;

any terminal methyl moiety present in R^2 and R^5 is optionally replaced with -CH_2OH, CF_3, -CH_2F, -CH_2Cl, C(O)CH_3, C(O)CF_3, CN, or CO_2H;

R^7 and R^8 are each independently selected from hydrogen and C_1-C_6 alkyl; and

Q is selected from aryl, heteroaryl, carbocyclyl and heterocyclyl, any of which is optionally substituted; wherein

R^1 and R^3 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

R^4 and R^6 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

R^1 and R^2 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl; or

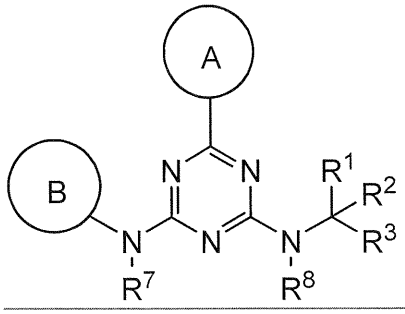
R^4 and R^5 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl, an optionally substituted 5-6 member monocyclic aryl, or an optionally substituted heteroaryl;

wherein:

(i) when X is CH and A is optionally substituted 1-imidazolyl, optionally substituted 1-pyrrolyl or optionally substituted 1-pyrazolyl, then neither N(R^7)C(R^4)(R^5)(R^6) nor N(R^8)C(R^1)(R^2)(R^3) is NH(CH_2)$_7CH_3$, NHCH_2-(o-chloro-phenyl), or NHCH_2CH_2OH; and

(ii) when X and X^c are both N, then neither $N(R^7)C(R^4)(R^5)(R^6)$ nor $N(R^8)C(R^1)(R^2)(R^3)$ is $N(CH_3)_2$, $NHCH_3$, or $N(CH_2CH_3)_2$.

In still another aspect, there is provided a compound having Formula III, or pharmaceutically acceptable salt or hydrate thereof:



(III), wherein:

ring A is an optionally substituted 5-6 member monocyclic heteroaryl;

ring B is an optionally substituted 5-6 member monocyclic aryl or monocyclic heteroaryl;

R^1 and R^3 are each independently selected from hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, -O-C_1-C_4 alkyl, and CN, wherein each said alkyl moiety of R^1, R^3, R^4, and R^6 are each independently optionally substituted with -OH, $-NH_2$, -CN, -O-C_1-C_4 alkyl, -NH(C_1-C_4 alkyl), or -N(C_1-C_4 alkyl)$_2$;

R^2 is selected from: -(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-C(O)-NH_2, -(C_1-C_6 alkyl)-CO_2H, -(C_2-C_6 alkenyl or alkynyl), -(C_1-C_6 alkylene)-O-(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-C(O)N(R^6)-(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-Q, -(C_0-C_6 alkylene)-C(O)-(C_1-C_6 alkyl), and -(C_0-C_6 alkylene)-C(O)-(C_0-C_6 alkylene)-Q, wherein:

any alkyl or alkylene moiety present in R^2 is optionally substituted with one or more -OH, -O(C_1-C_4 alkyl), -CO_2H, or halo;

any terminal methyl moiety present in R^2 is optionally replaced with -CH_2OH, CF_3, -CH_2F, -CH_2Cl, $C(O)CH_3$, $C(O)CF_3$, CN, or CO_2H;

R^7 and R^8 are each independently selected from hydrogen and C_1-C_6 alkyl; and

Q is selected from aryl, heteroaryl, carbocyclyl and heterocyclyl, any of which is optionally substituted; wherein

R^1 and R^3 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

R^1 and R^2 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl;

wherein when A is an oxadiazole substituted with an optionally substituted pyridinyl, then G is not an optionally substituted phenyl.

The compounds of Formula I, Ia, Ib, B, C, Ic, Id, Ie, If, Ig, II, III, IIIa, IIIb, IIIc, and IIId, or as described in any one of the embodiments herein inhibits mutant IDH1or mutant IDH2. Also described herein are pharmaceutical compositions comprising a compound of Formula I, Ia, Ib, B, C, Ic, Id, Ie, If, Ig, II, III, IIIa, IIIb, IIIc, and IIId, and methods of using such compositions to treat cancers characterized by the presence of a mutant IDH1 or mutant IDH2. In an aspect, there is provided a pharmaceutical composition comprising a compound as disclosed above, and a pharmaceutically acceptable carrier. In another aspect, there is provided the use of a compound or pharmaceutical composition as disclosed above in the manufacture of a medicament for the treatment of a cancer characterized by the presence of an IDH1 mutation, wherein the IDH1 mutation results in a new ability of the enzyme to catalyze the NAPH-dependent reduction of α-ketoglutarate to *R*(-)-2-hydroxyglutarate in a patient.

DETAILED DESCRIPTION

The details of construction and the arrangement of components set forth in the following description or illustrated in the drawings are not meant to be limiting. Other embodiments and different ways to practice the invention are expressly included. Also, the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting. The use of "including," "comprising," or "having," "containing", "involving", and variations thereof herein, is meant to encompass the items listed thereafter and equivalents thereof as well as additional items.

Definitions:

The term "halo" or "halogen" refers to any radical of fluorine, chlorine, bromine or iodine.

any terminal methyl moiety present in R^2 is optionally replaced with $-CH_2OH$, CF_3, $-CH_2F$, $-CH_2Cl$, $C(O)CH_3$, $C(O)CF_3$, CN, or CO_2H;
R^7 and R^8 are each independently selected from hydrogen and C_1-C_6 alkyl; and
Q is selected from aryl, heteroaryl, carbocyclyl and heterocyclyl, any of which is optionally substituted; wherein
R^1 and R^3 are optionally taken together with the carbon atom to which they are attached to form C(=O); or
R^1 and R^2 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl;
wherein when A is an oxadiazole substituted with an optionally substituted pyridinyl, then G is not an optionally substituted phenyl.

12. The compound of claim 11, wherein G is substituted with 1 or 2 substituents selected from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, -CN, =O, -OH, aryl, heteroaryl -SO_2C_1-C_4 alkyl, $-CO_2C_1$-C_4 alkyl, -C(O)aryl, and $-C(O)C_1$-C_4 alkyl.

13. A pharmaceutical composition comprising a compound of claim 1, and a pharmaceutically acceptable carrier.

14. The composition of claim 13, further comprising a second therapeutic agent useful in the treatment of cancer.

15. A method of treating a cancer characterized by the presence of an IDH1 mutation, wherein the IDH1 mutation results in a new ability of the enzyme to catalyze the NAPH-dependent reduction of α-ketoglutarate to *R*(-)-2-hydroxyglutarate in a patient, comprising the step of administering to the patient in need thereof a composition of claim 13.

16. The method of claim 15, wherein the IDH1 mutation is an IDH1 R132H or R132C mutation.

17. The method of claim 16, wherein the cancer is selected from from glioma (glioblastoma), acute myelogenous leukemia, sarcoma, melanoma, non-small cell lung cancer (NSCLC), cholangiocarcinomas, chondrosarcoma, myelodysplastic syndromes (MDS), myeloproliferative neoplasm (MPN), colon cancer,or angio-immunoblastic non-Hodgkin's lymphoma (NHL) in a patient.

18. The method of claims 16, further comprising administering to the patient in need thereof a second therapeutic agent useful in the treatment of cancer.

any terminal methyl moiety present in R^2 is optionally replaced with $-CH_2OH$, CF_3, $-CH_2F$, $-CH_2Cl$, $C(O)CH_3$, $C(O)CF_3$, CN, or CO_2H;

R^7 and R^8 are each independently selected from hydrogen and C_1-C_6 alkyl; and

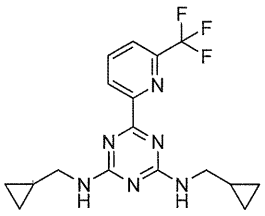
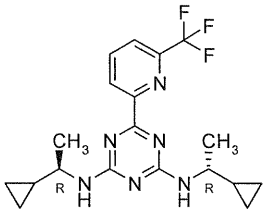
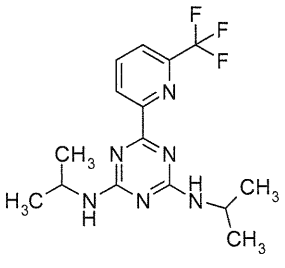
Q is selected from aryl, heteroaryl, carbocyclyl and heterocyclyl, any of which is optionally substituted; wherein

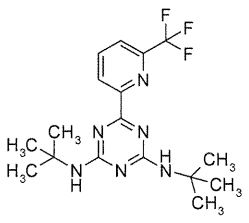
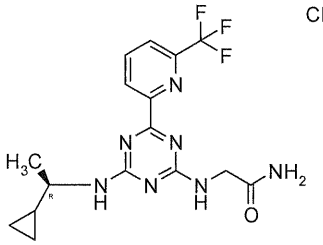
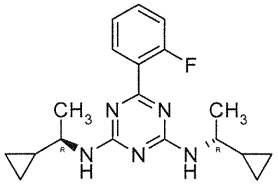
R^1 and R^3 are optionally taken together with the carbon atom to which they are attached to form C(=O); or

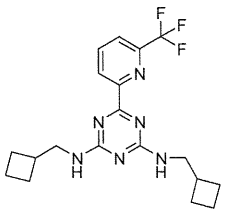
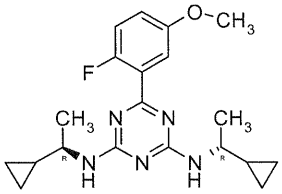
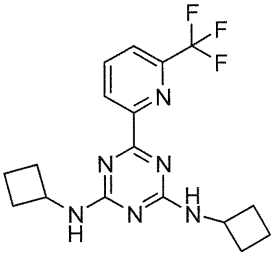
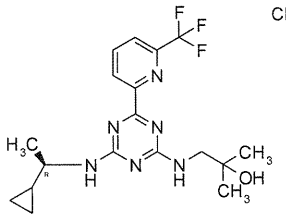
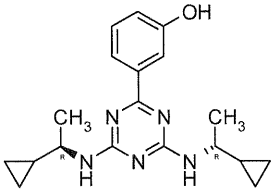
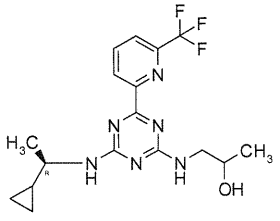
R^1 and R^2 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl;

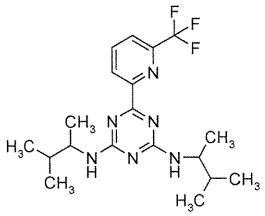
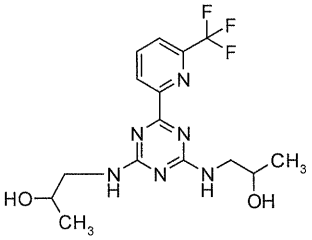
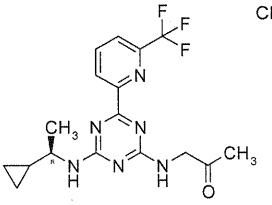
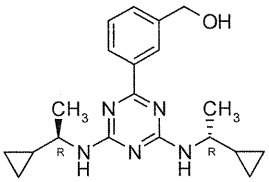
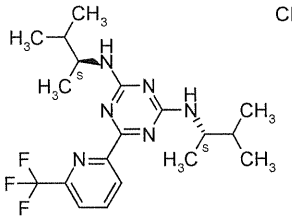
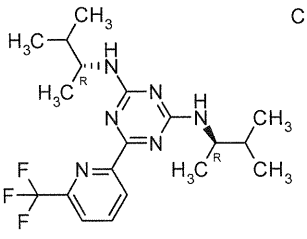
wherein when A is an oxadiazole substituted with an optionally substituted pyridinyl, then G is not an optionally substituted phenyl.

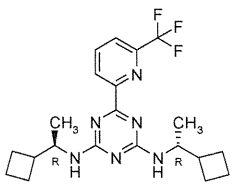
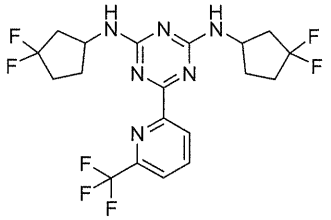
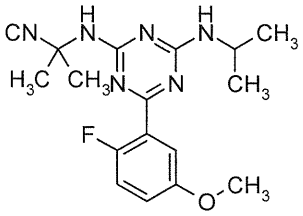
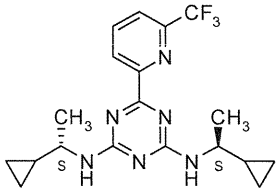
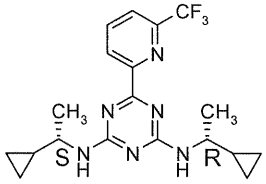
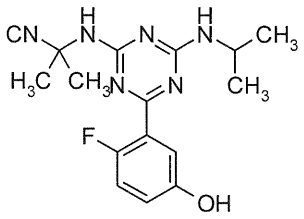
12. The compound according to claim 1, selected from the group consisting of:

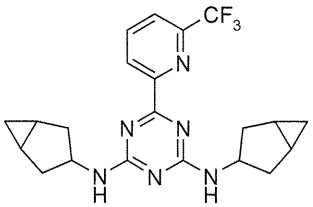
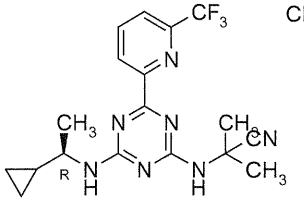
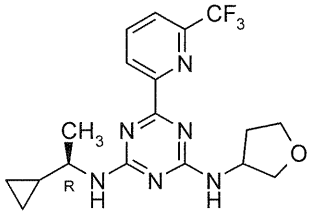
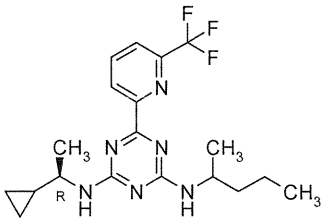
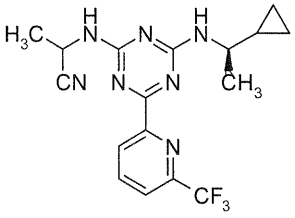
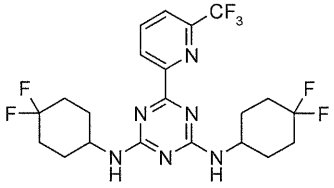
1	
2	 Chiral
3	

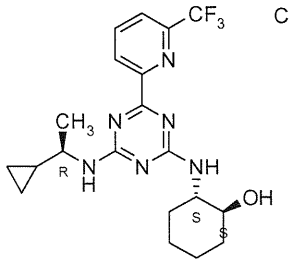
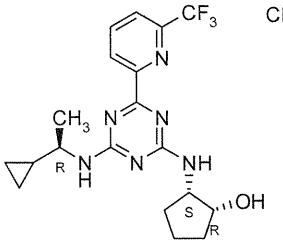
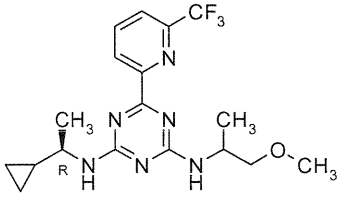
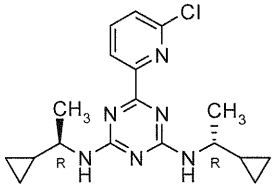
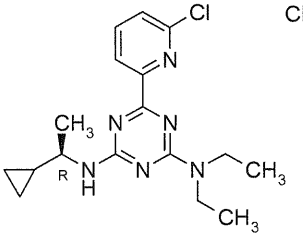
4	
5	 Chiral
6	 Chiral

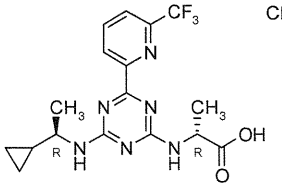
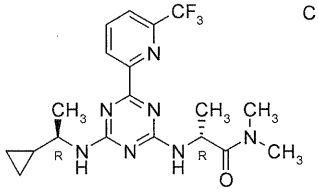
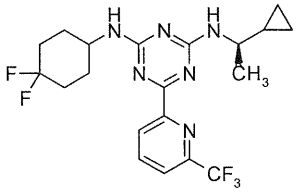
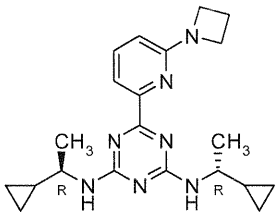
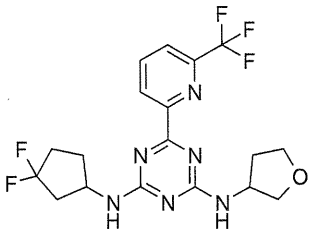
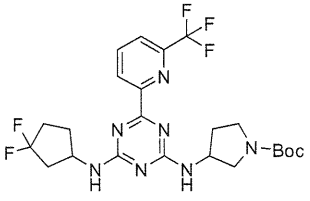
7	
8	 Chiral
9	
10	 Chiral
11	 Chiral
12	

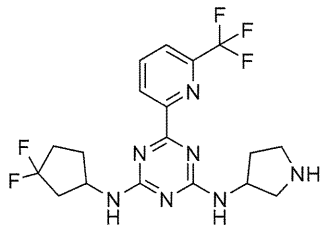
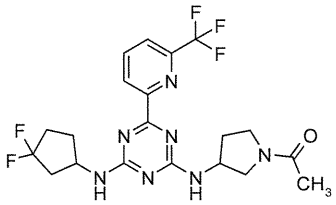
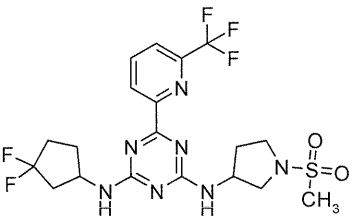
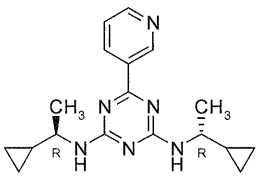
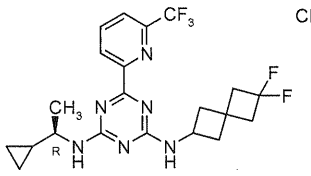
13	
14	
15	 Chiral
16	 Chiral
17	 Chiral
18	 Chiral

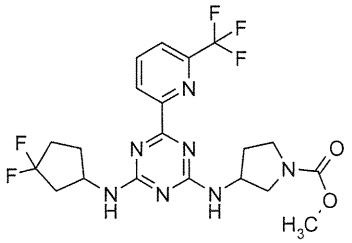
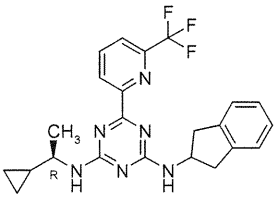
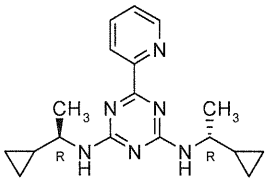
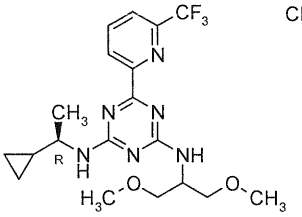
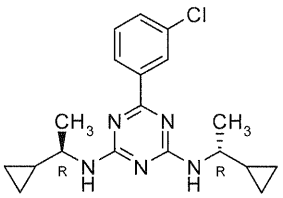
19	 Chiral
31	
32	
33	 Chiral
34	 Chiral
35	

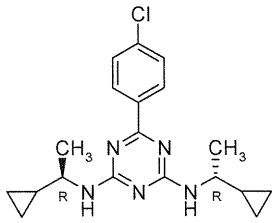
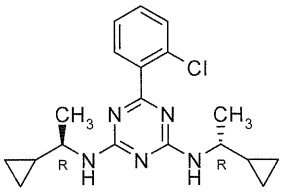
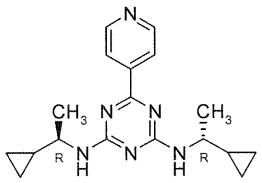
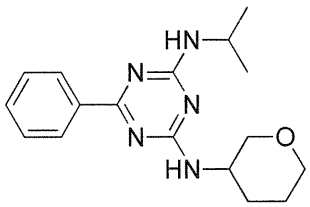
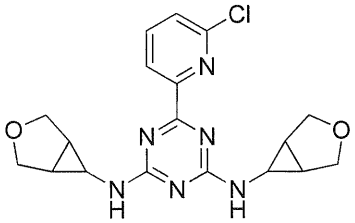
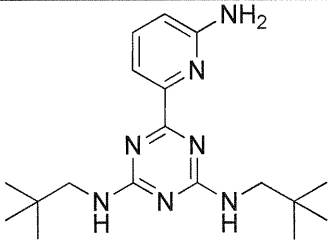
36	
37	 Chiral
38	
39	
40	
41	

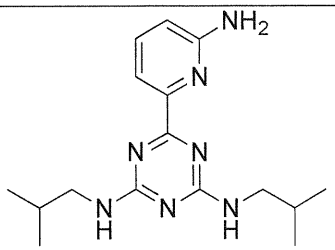
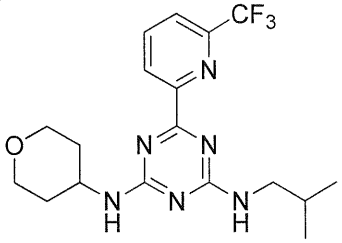
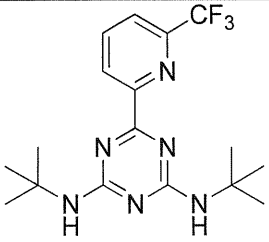
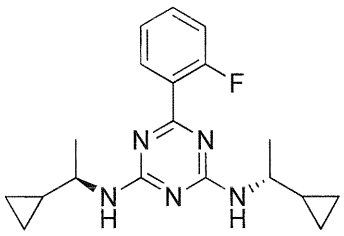
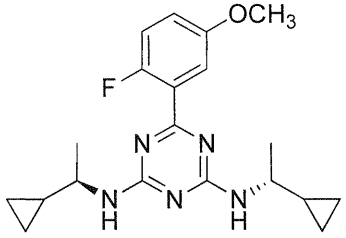
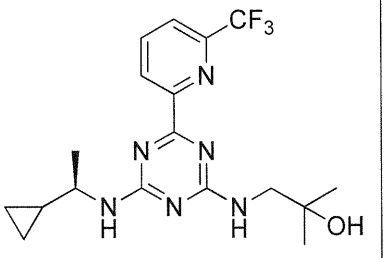
42	 Chiral
43	 Chiral
44	
45	 Chiral
46	 Chiral

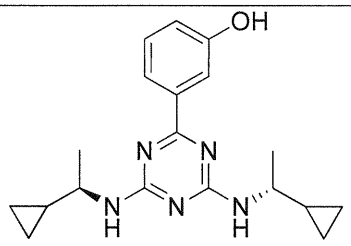
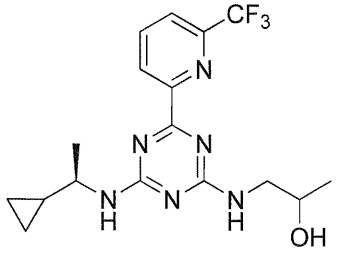
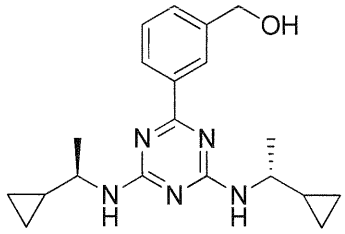
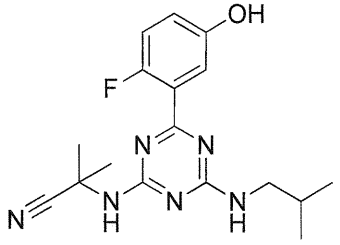
47	 Chiral
48	 Chiral
50	 Chiral
51	 Chiral
52	
53	

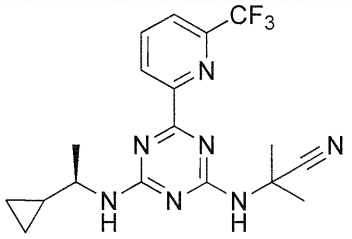
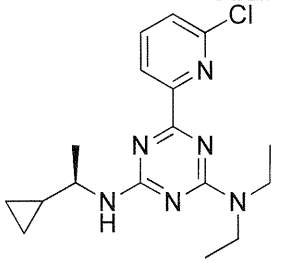
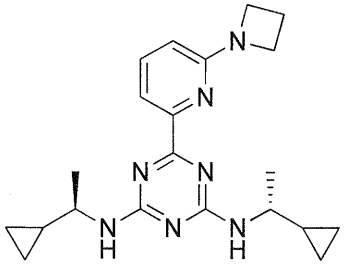
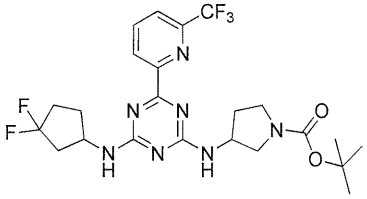
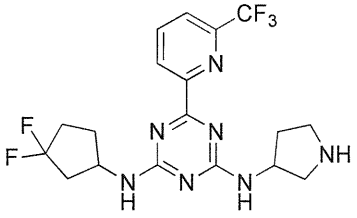
54	
55	
56	
57	Chiral 
58	Chiral 

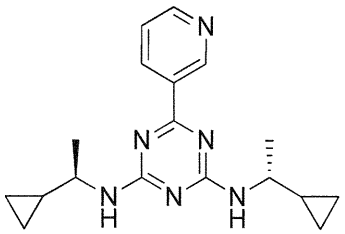
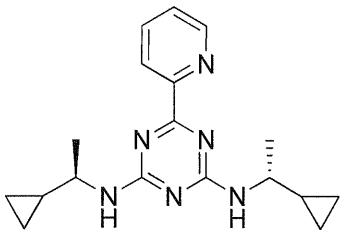
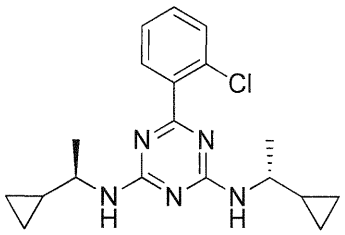
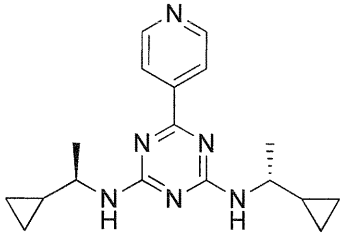
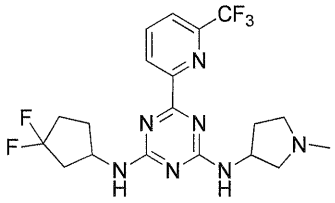
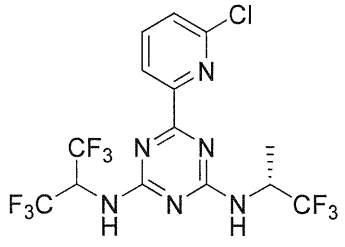
59	
60	Chiral 
61	Chiral 
63	Chiral 
64	Chiral 

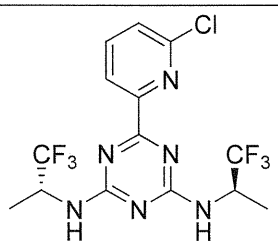
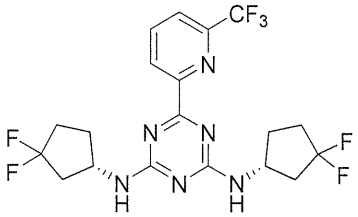
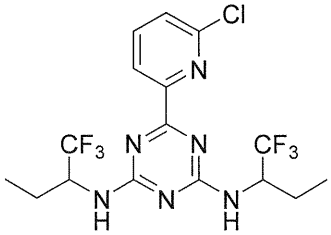
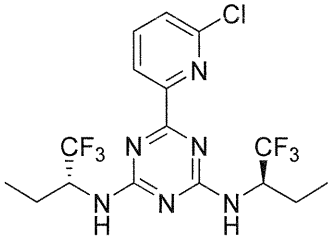
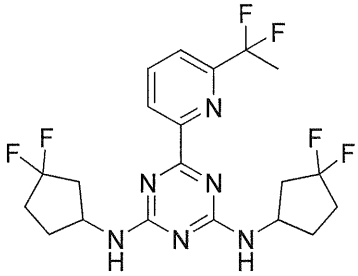
65	 Chiral
66	 Chiral
67	 Chiral
69	
72	
73	

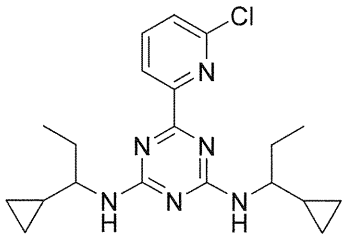
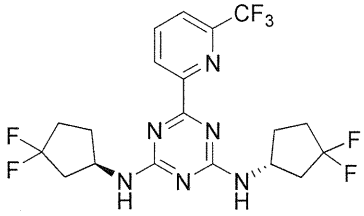
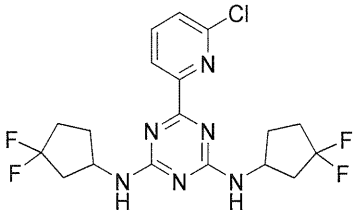
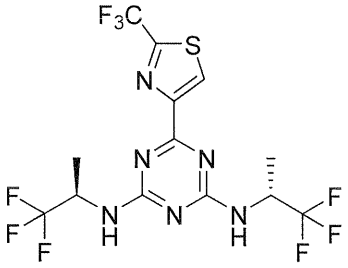
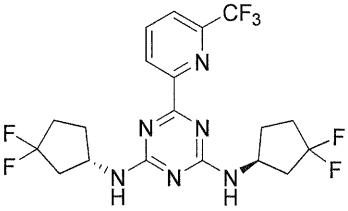
74	
75	
76	
77	
78	
79	

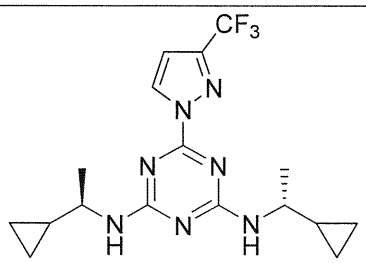
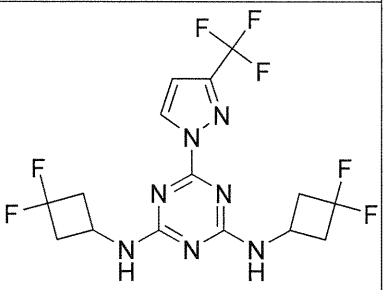
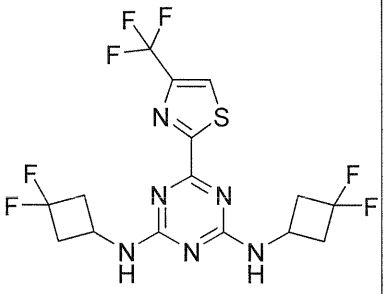
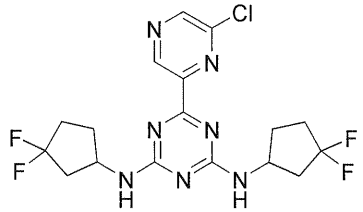
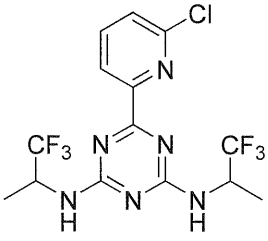
80	
81	
82	
86	

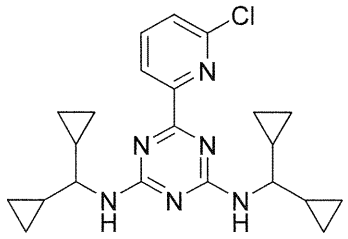
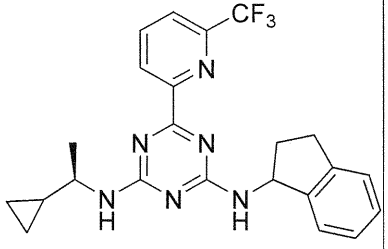
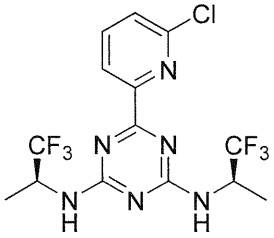
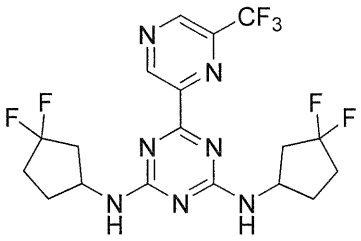
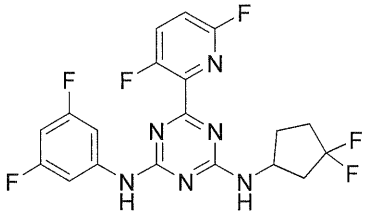
87	
88	
89	
90	
91	

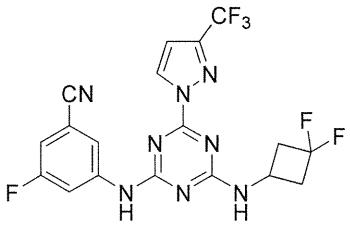
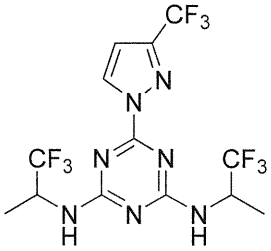
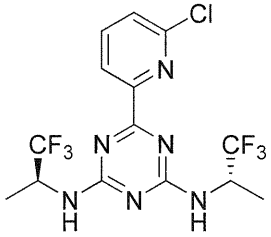
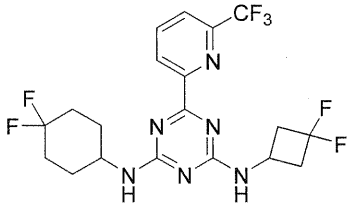
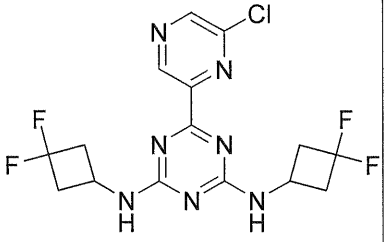
92	
93	
94	
95	
96	
100	

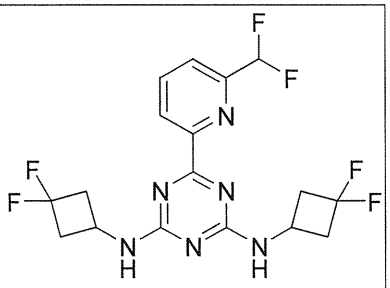
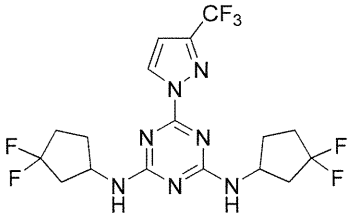
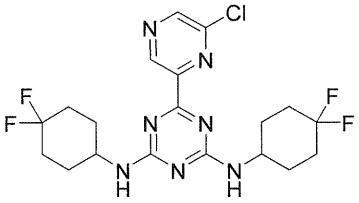
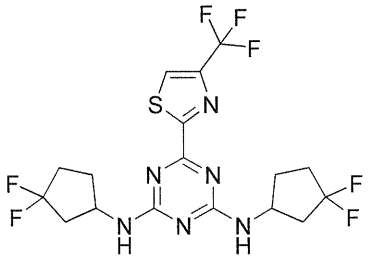
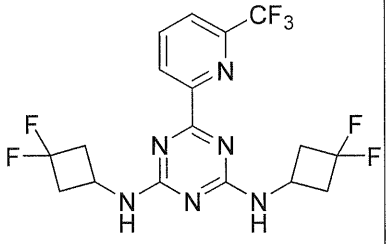
101	
102	
103	
104	
105	

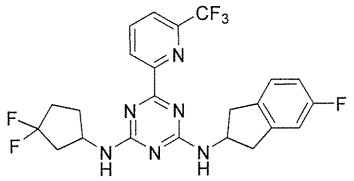
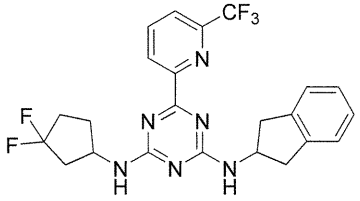
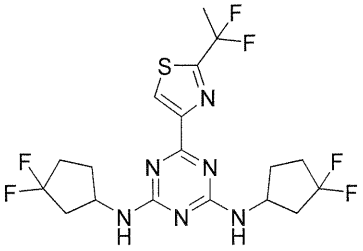
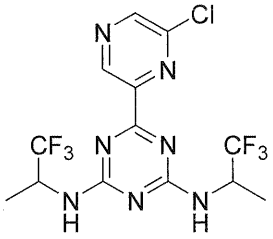
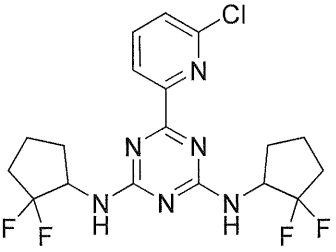
110	
111	
113	
114	
118	

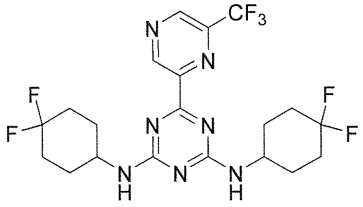
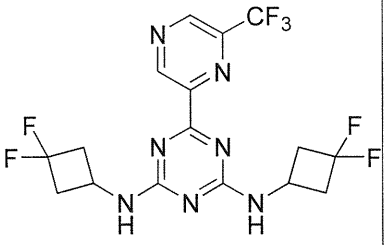
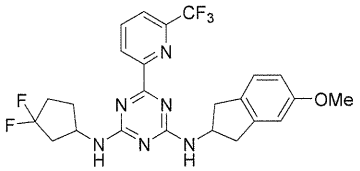
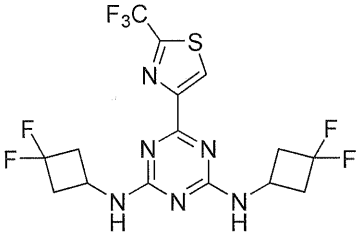
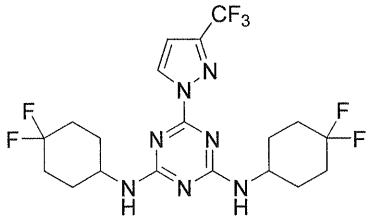
121	
126	
128	
129	
130	

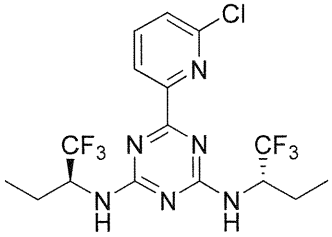
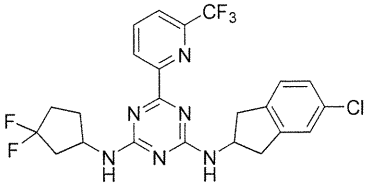
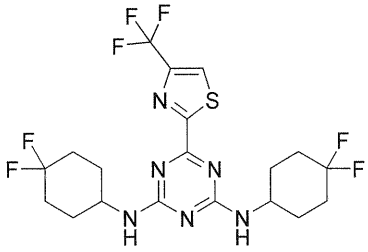
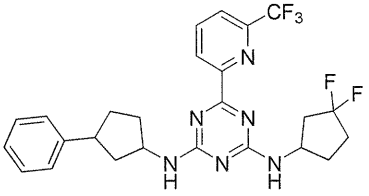
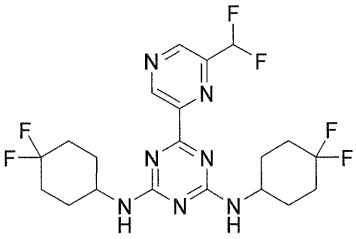
131	
135	
136	
138	
139	

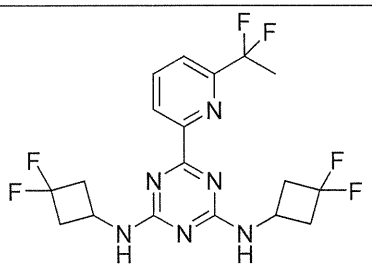
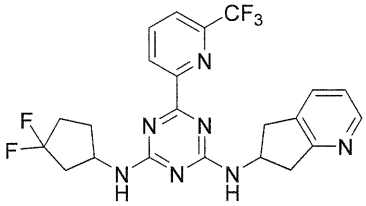
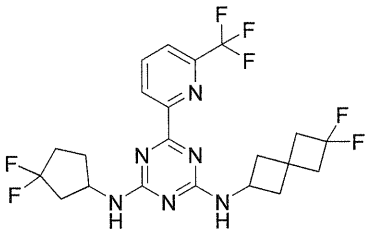
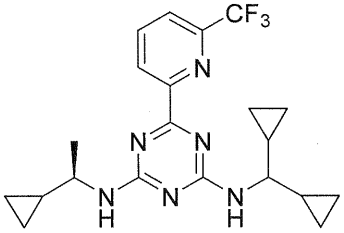
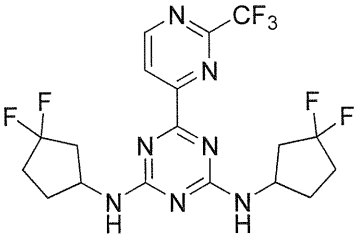
140	
141	
142	
143	
144	

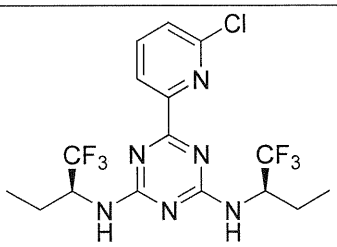
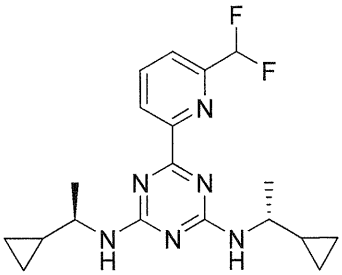
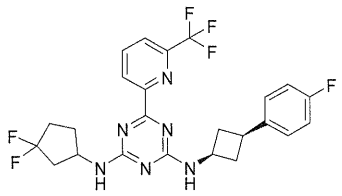
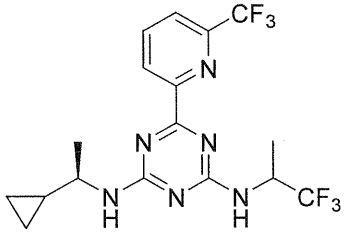
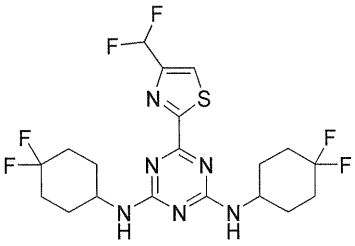
145	
146	
147	
148	
149	

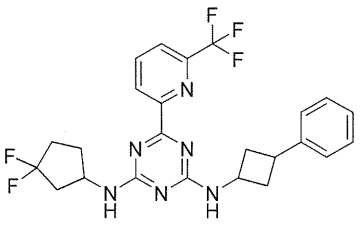
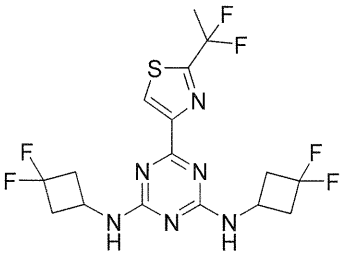
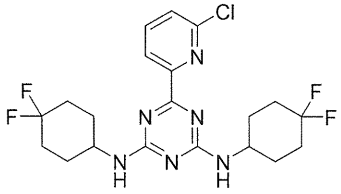
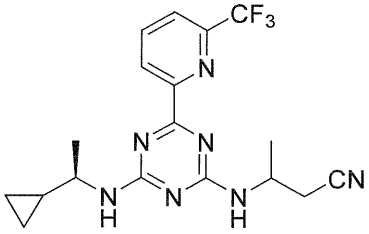
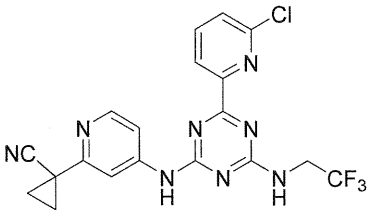
150	
152	
155	
156	
157	

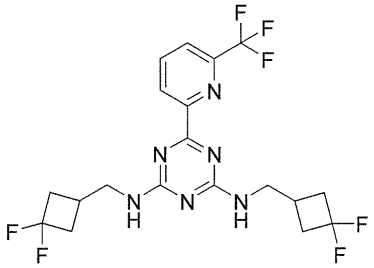
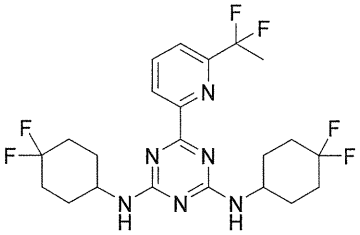
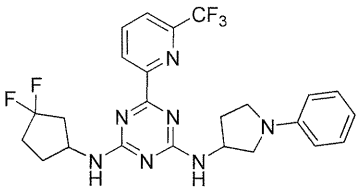
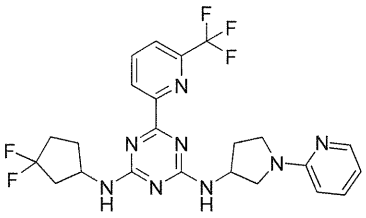
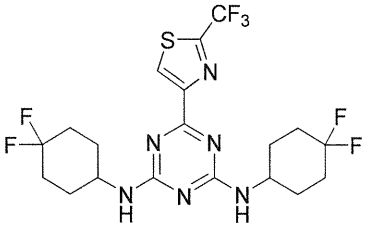
160	
161	
166	
170	
176	

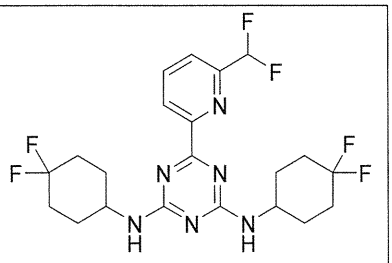
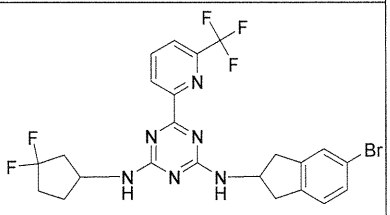
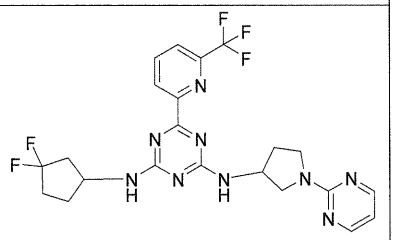
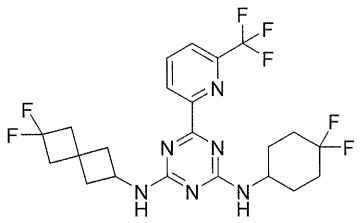
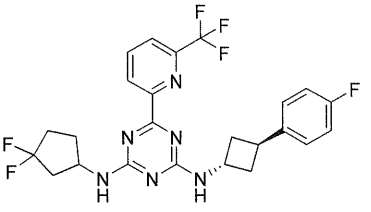
180	
182	
183	
184	
186	

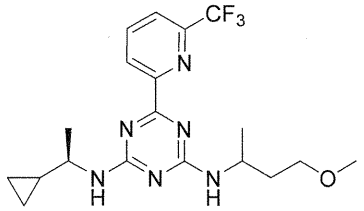
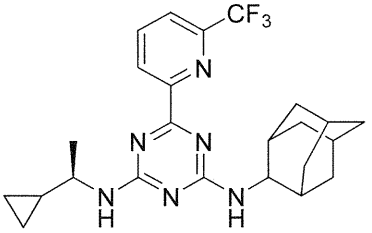
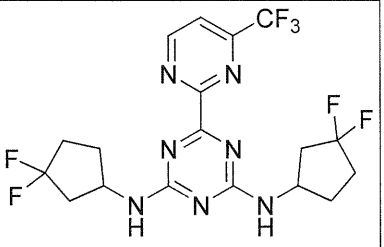
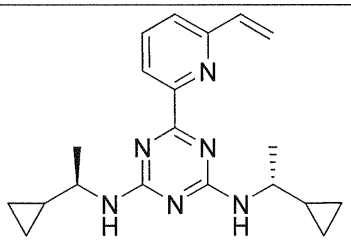
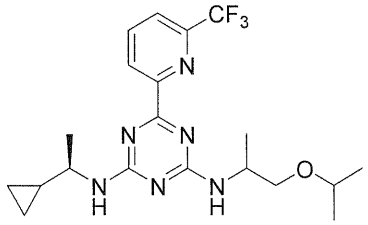
187	
188	
191	
193	
194	

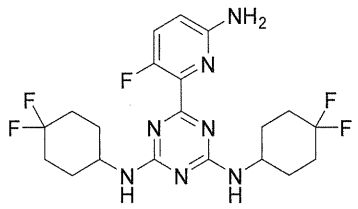
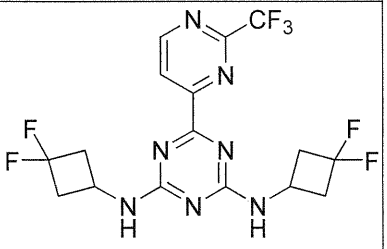
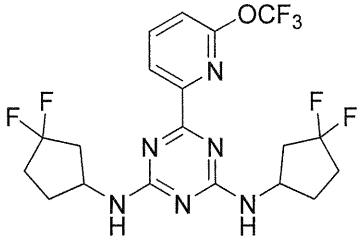
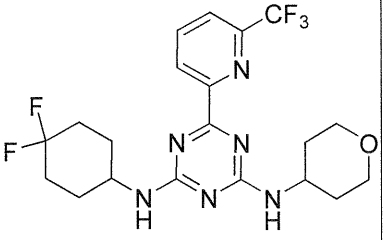
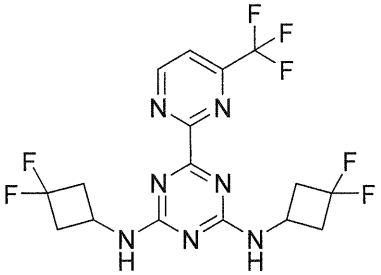
196	
198	
199	
203	
205	

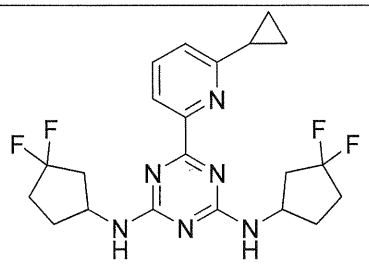
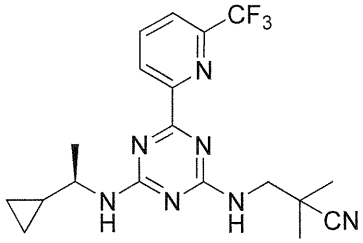
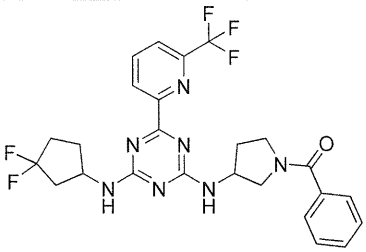
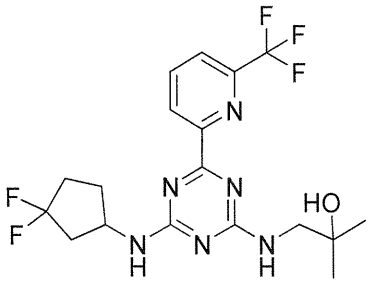
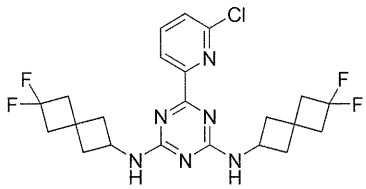
208	
209	
212	
214	
215	

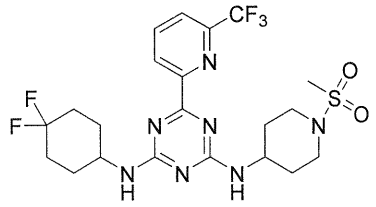
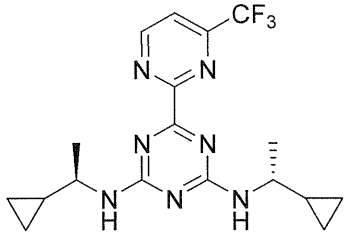
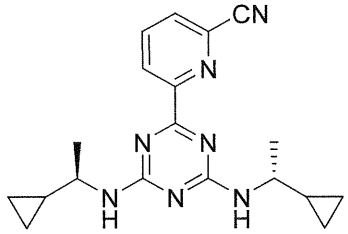
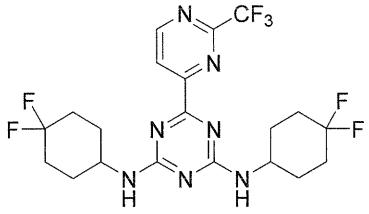
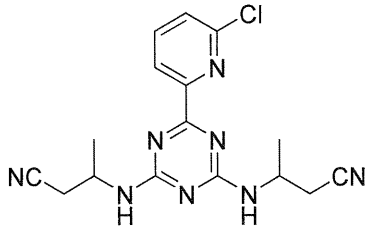
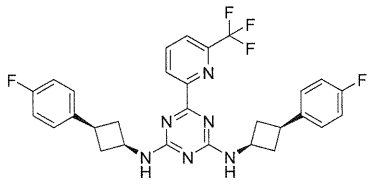
216	
218	
219	
222	
223	

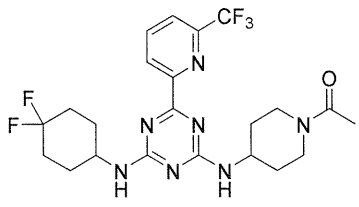
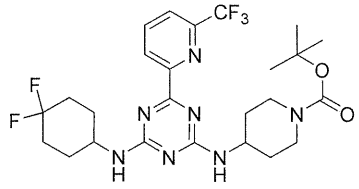
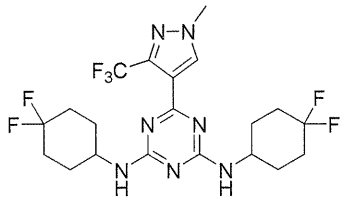
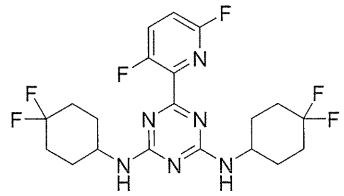
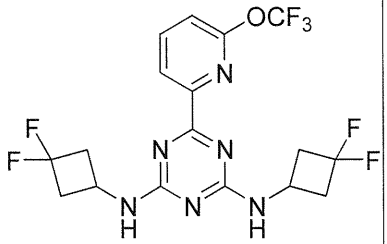
224	
225	
227	
228	
230	

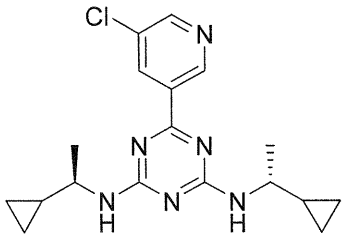
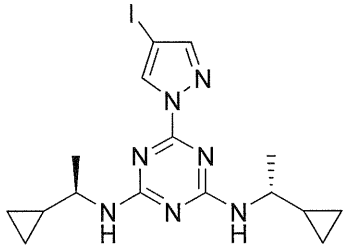
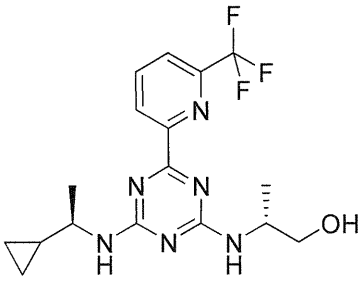
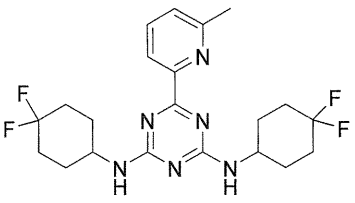
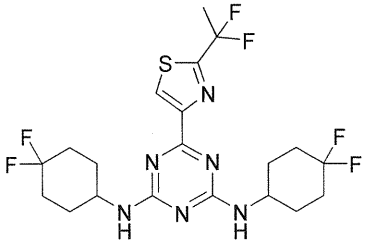
233	
234	
237	
240	
241	

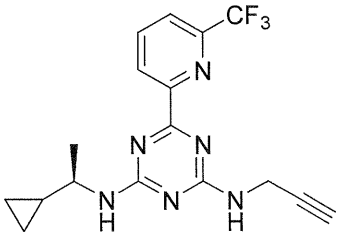
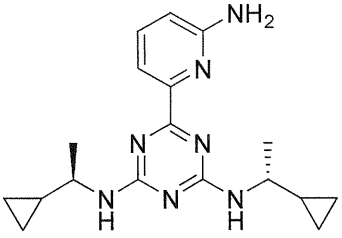
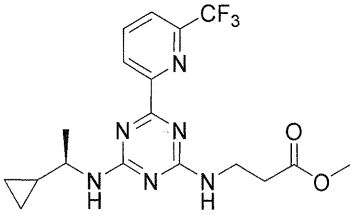
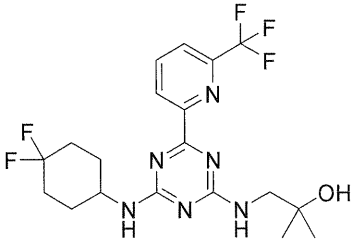
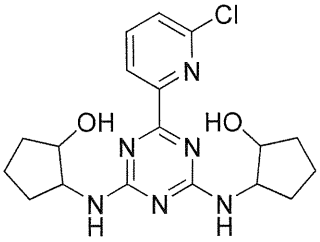
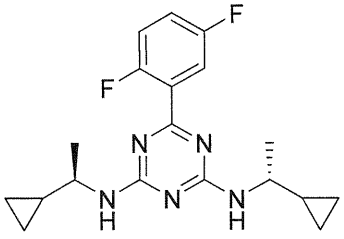
249	
251	
252	
255	
256	

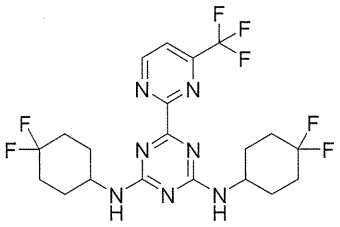
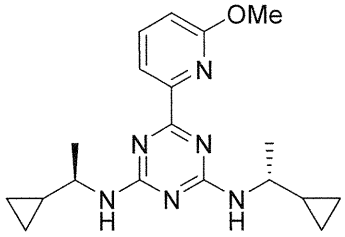
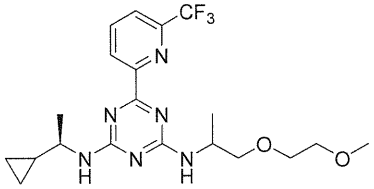
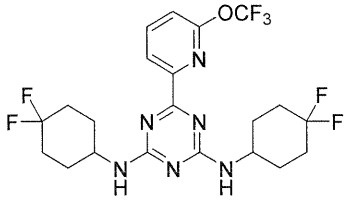
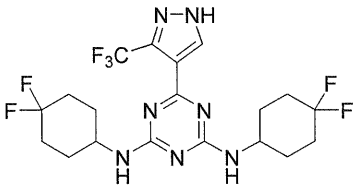
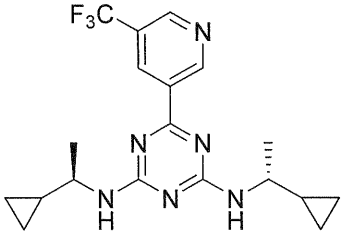
258	
262	
263	
264	
265	

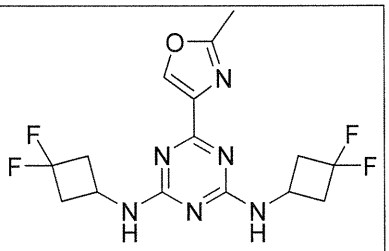
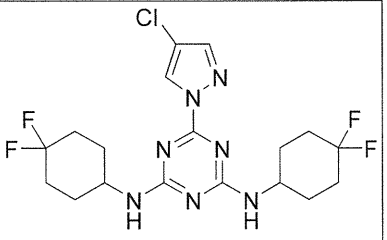
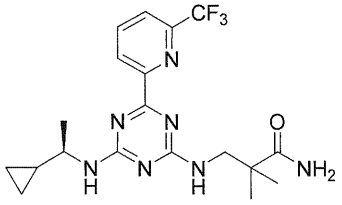
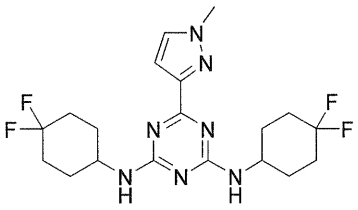
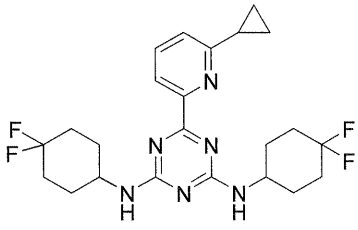
266	
268	
269	
270	
271	
272	

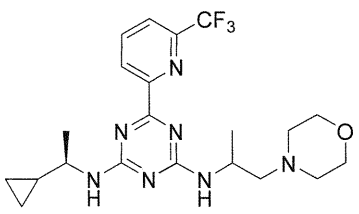
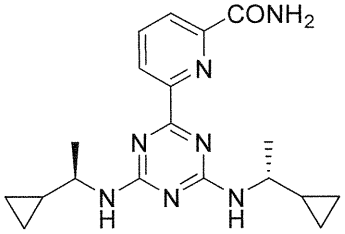
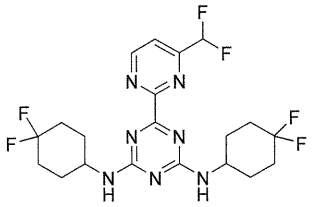
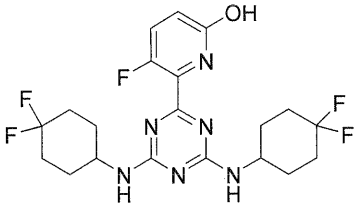
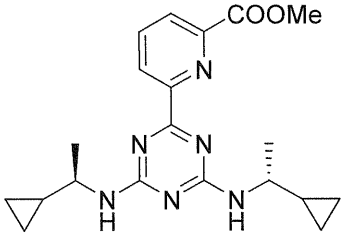
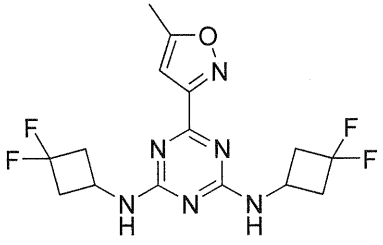
273	
274	
275	
276	
277	

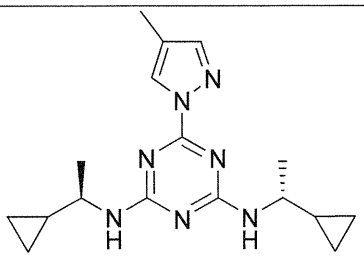
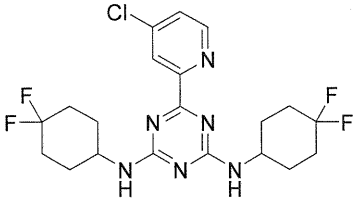
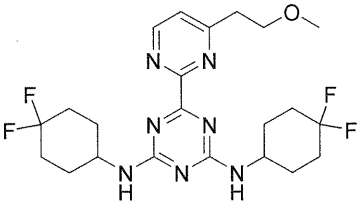
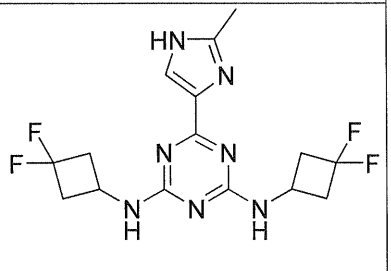
278	
279	
281	
282	
283	

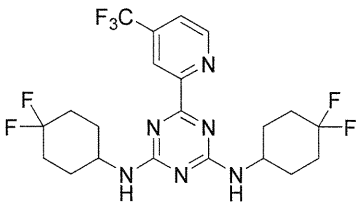
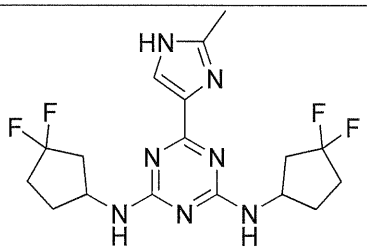
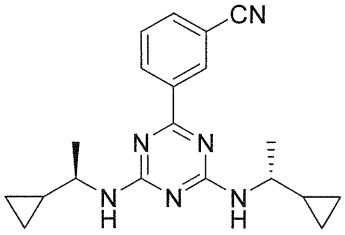
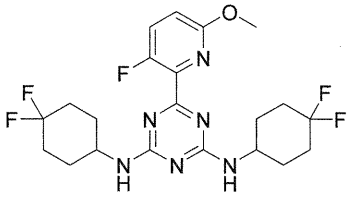
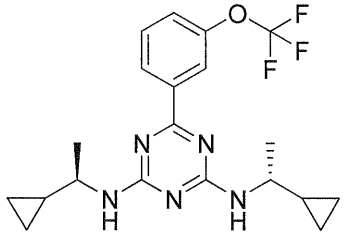
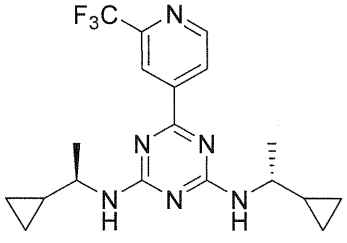
284	
285	
286	
287	
290	
292	

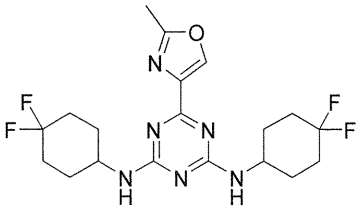
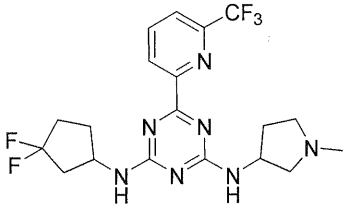
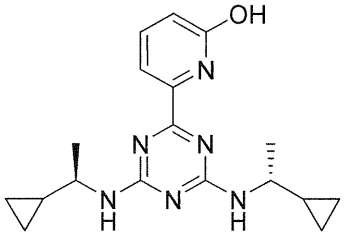
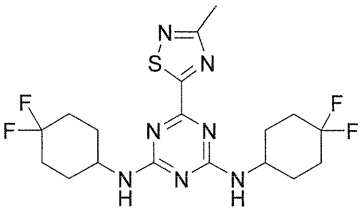
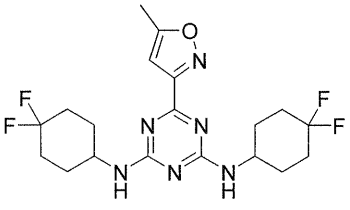
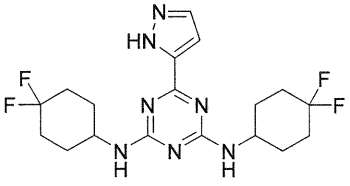
293	
294	
295	
296	
297	
300	

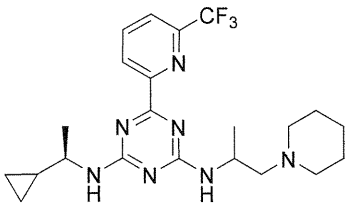
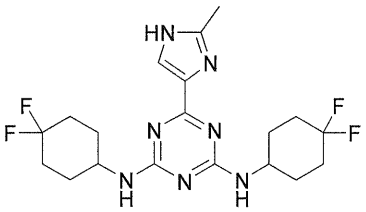
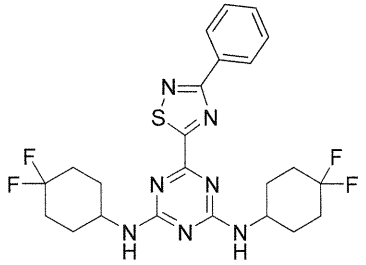
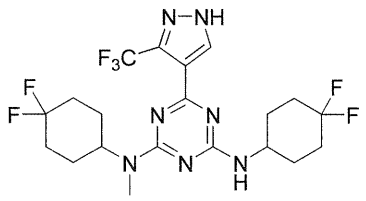
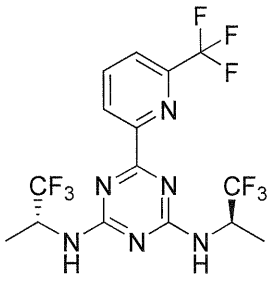
301	
302	
303	
304	
305	

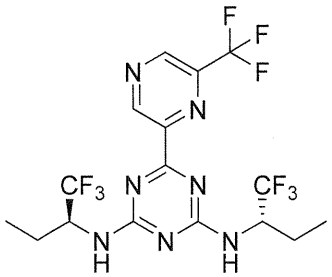
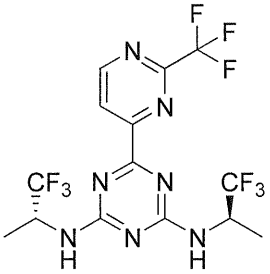
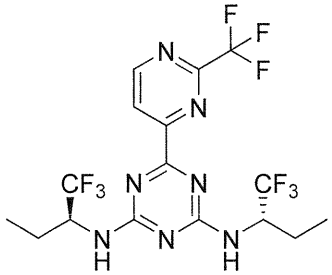
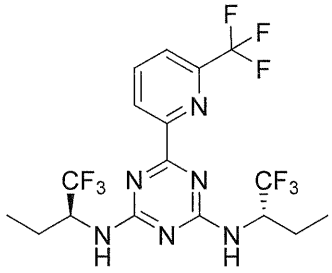
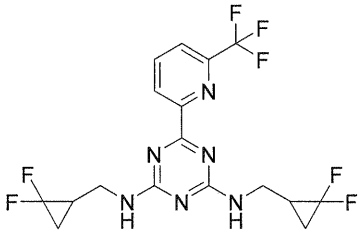
306	
307	
308	
309	
310	
311	

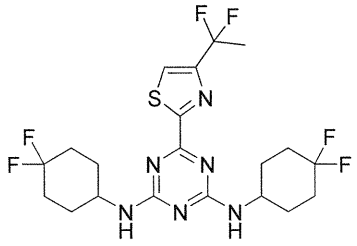
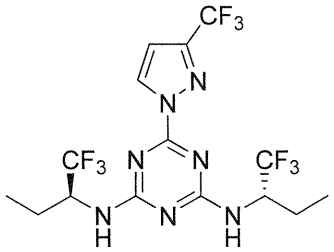
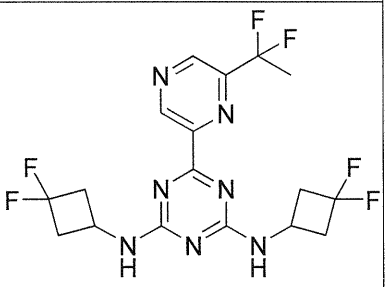
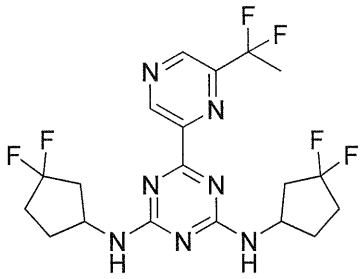
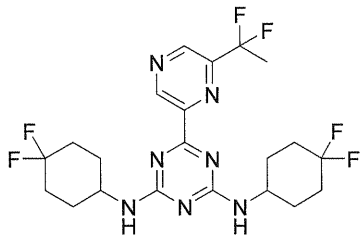
312	
314	
315	
317	

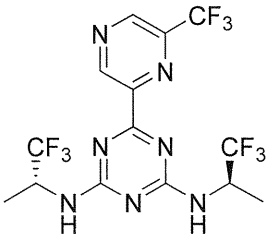
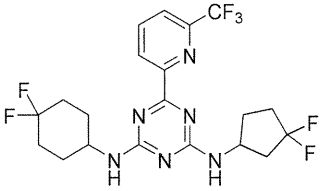
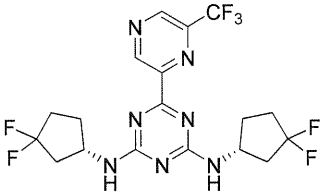
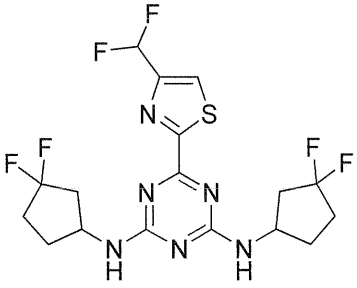
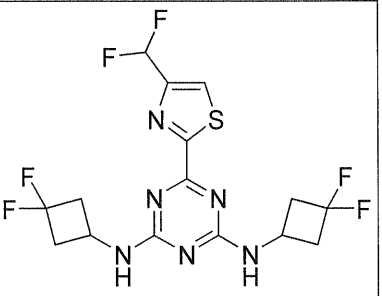
318	
319	
320	
321	
322	
323	

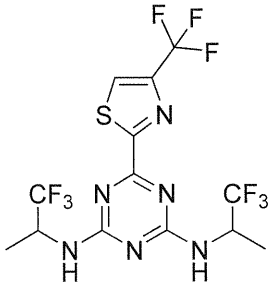
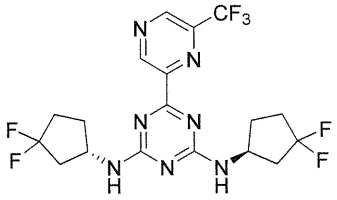
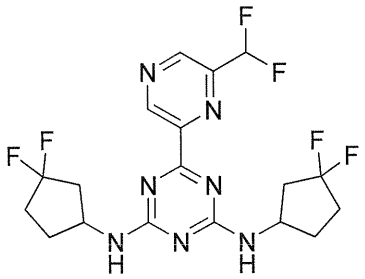
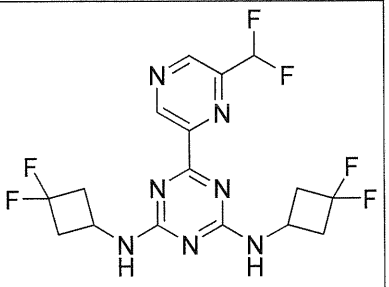
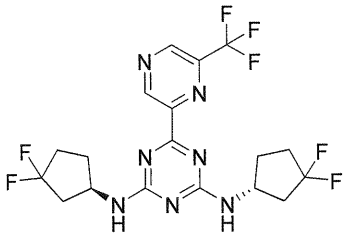
324	
326	
327	
328	
329	
330	

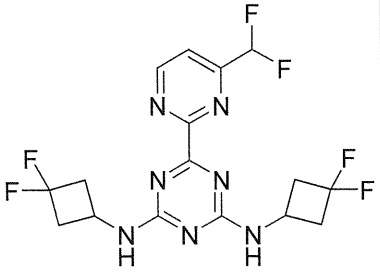
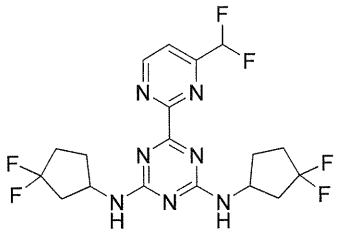
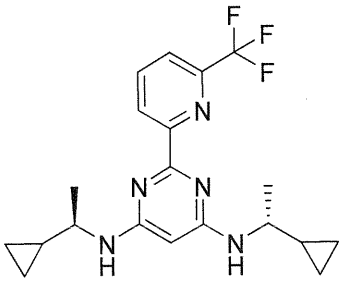
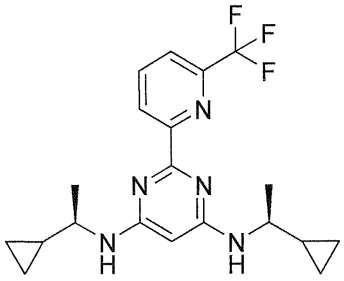
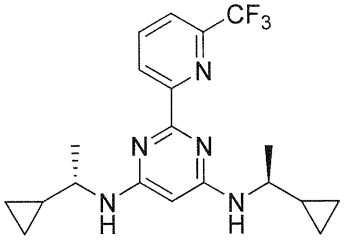
331	
332	
333	
334	
335	

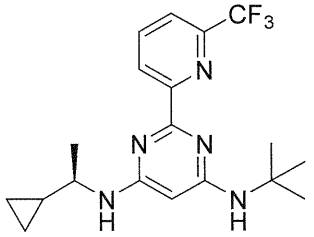
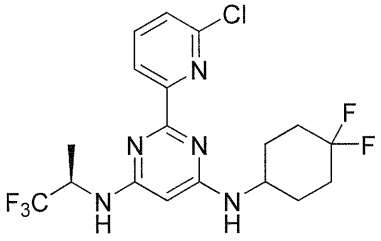
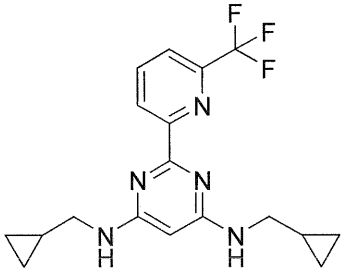
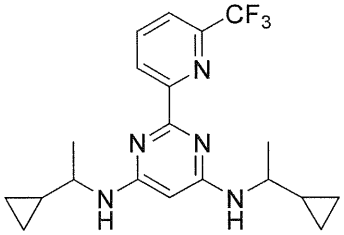
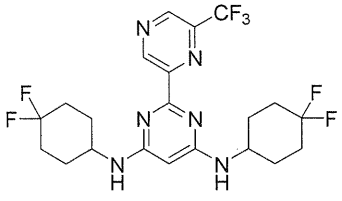
339	
344	
345	
346	
354	

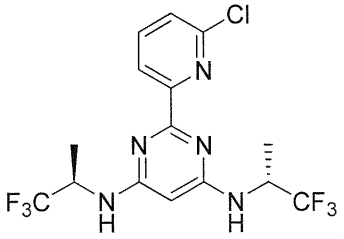
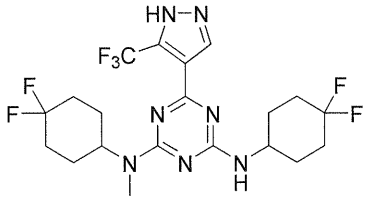
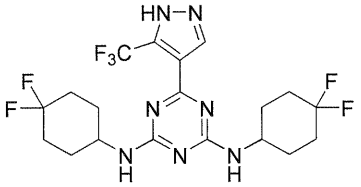
357	
363	
366	
370	
374	

386	
395	
399	
402	
403	

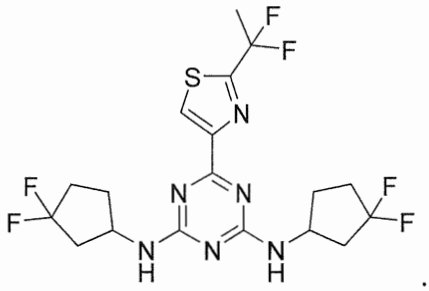
404	
406	
408	
409	
410	

411	
412	
414	
415	
416	

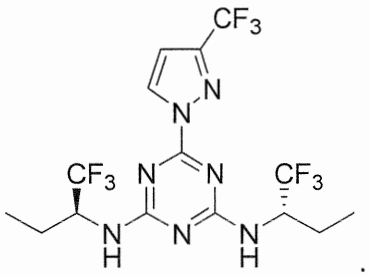
417	
418	
419	
420	
421	

422	
423	
424	 and

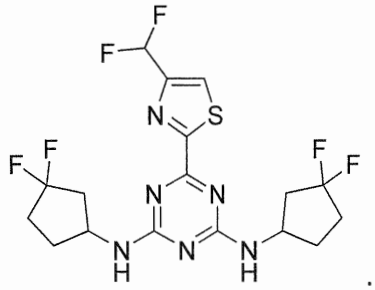
13. The compound of claim 1, having the structure:



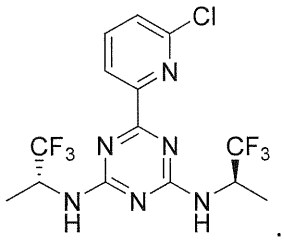
14. The compound of claim 1, having the structure:



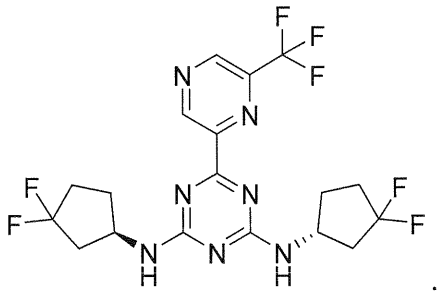
15. The compound of claim 1, having the structure:



16. The compound of claim 1, having the structure:



17. The compound of claim 1, having the structure:



18. A pharmaceutical composition comprising a compound of any one of claims 1 to 17, and a pharmaceutically acceptable carrier.

19. The pharmaceutical composition of claim 18, further comprising a second therapeutic agent useful in the treatment of cancer.

20. Use of a compound or pharmaceutical composition of any one of claims 1 to 19 in the manufacture of a medicament for the treatment of a cancer characterized by the presence of an IDH1 mutation, wherein the IDH1 mutation results in a new ability of the enzyme to catalyze the NAPH-dependent reduction of α-ketoglutarate to *R*(-)-2-hydroxyglutarate in a patient.

21. The use of claim 20, wherein the IDH1 mutation is an IDH1 R132H or R132C mutation.

22. The use of claim 21, wherein the cancer is selected from glioma (glioblastoma), acute myelogenous leukemia, sarcoma, melanoma, non-small cell lung cancer (NSCLC), cholangiocarcinomas, chondrosarcoma, myelodysplastic syndromes (MDS), myeloproliferative neoplasm (MPN), colon cancer, or angio-immunoblastic non-Hodgkin's lymphoma (NHL) in a patient.

23. The use of claim 22, wherein the cancer is glioma.