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]-;

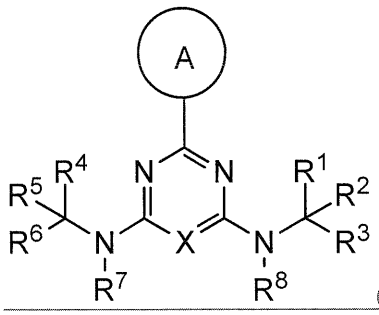
(43) α,α'-[(6-phenyl-1,3,5-triazine-2,4-diyl)bis[imino(1,1,2,2-tetrafluoro-3-oxo-3,1-propanediyl)]]bis[ω-[tetrafluoro(trifluoromethyl)ethoxy]-Poly[oxy[trifluoro(trifluoromethyl)-1,2-ethanediyl]];

(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)$NHCH_2R$, 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,

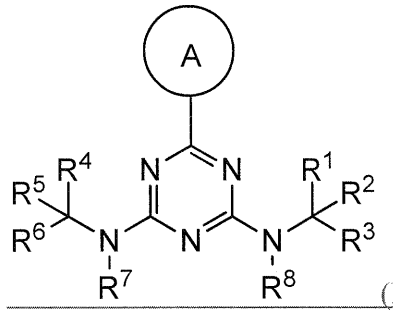
(41) N-[4-[[5-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenyl]amino]-6-(5-thiazolyl)-1,3,5-triazin-2-yl]-L-Valine,

(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-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 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,

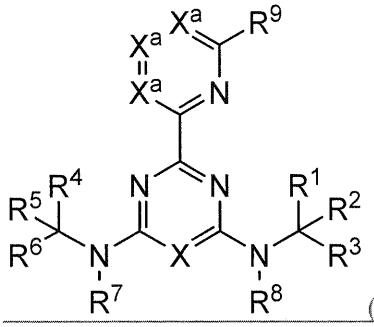
(37) N-[4-[[5-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenyl]amino]-6-(5-thiazolyl)-1,3,5-triazin-2-yl]-L-Valine,

(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-;

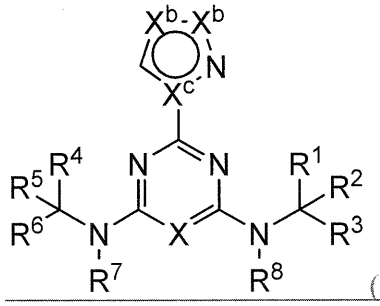
(2) 4,6-Pyrimidinediamine, N4-ethyl-2-(6-methyl-2-pyridinyl)-N6-propyl-;

(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

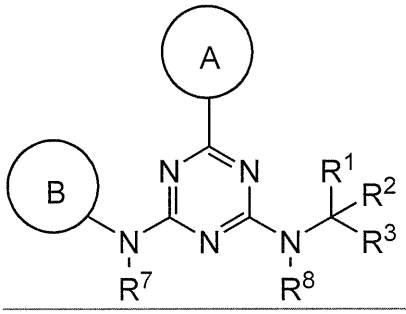
R^4 and R^5 are optionally taken together to form an optionally substituted carbocyclyl or optionally substituted heterocyclyl, an optionally substituted 5-6 member monocyclic aryl, or an optionally substituted heteroaryl;

wherein:

(i) when X is CH and A is optionally substituted l-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 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~~ Use of a composition of claim 13 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.

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

17. The ~~method~~ use 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~~ use of claim~~s~~ 16, wherein the medicament is to be administered with ~~further comprising administering to the patient in need thereof~~ a second therapeutic agent useful in the treatment of cancer.