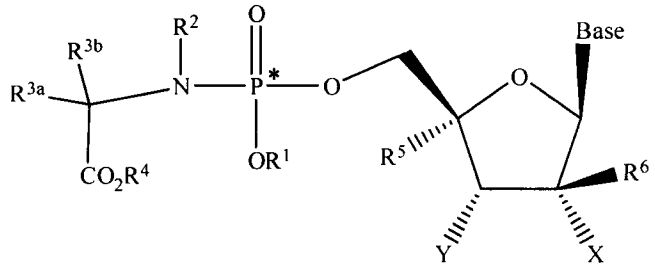
We claim:

1. A compound, its stereoisomer, salt, hydrate, solvate, or crystalline form thereof, represented by formula I:




I

wherein

(a) $R^1$ is hydrogen, n-alkyl; branched alkyl; cycloalkyl; or aryl, which includes, but is not limited to, phenyl or naphthyl, where phenyl or naphthyl are optionally substituted with at least one of $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{1-6}$ alkoxy, F, Cl, Br, I, nitro, cyano, $C_{1-6}$ haloalkyl, $-N(R^{1'})_2$, $C_{1-6}$ acylamino, $-NHSO_2C_{1-6}$ alkyl, $-SO_2N(R^{1'})_2$, $COR^{1''}$, and $-SO_2C_{1-6}$ alkyl; ($R^{1'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{1''}$ is –OR' or $-N(R^{1'})_2$);

(b) $R^2$ is hydrogen, $C_{1-10}$ alkyl, $R^{3a}$ or $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms, $C(O)CR^{3a}R^{3b}NHR^1$, where n is 2 to 4 and $R^1$, $R^{3a}$, and $R^{3b}$;

(c) $R^{3a}$ and $R^{3b}$ are (i) independently selected from hydrogen, $C_{1-10}$ alkyl, cycloalkyl, $-(CH_2)_c(NR^{3'})_2$, $C_{1-6}$ hydroxyalkyl, $-CH_2SH$, $-(CH_2)_2S(O)_dMe$, $-(CH_2)_3NHC(=NH)NH_2$, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, $-(CH_2)_eCOR^{3''}$, aryl and aryl $C_{1-3}$ alkyl, said aryl groups optionally substituted with a group selected from hydroxyl, $C_{1-10}$ alkyl, $C_{1-6}$ alkoxy, halogen, nitro and cyano; (ii) $R^{3a}$ and $R^{3b}$ both are $C_{1-6}$ alkyl; (iii) $R^{3a}$ and $R^{3b}$ together are$(CH_2)_f$ so as to form a spiro ring; (iv) $R^{3a}$ is hydrogen and $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms (v) $R^{3b}$ is hydrogen and $R^{3a}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that

includes the adjoining N and C atoms, where c is 1 to 6, d is 0 to 2, e is 0 to 3, f is 2 to 5, n is 2 to 4, and where $R^{3'}$ is independently hydrogen or $C_{1-6}$ alkyl and $R^{3''}$ is -OR' or $-N(R^{3'})_2$); (vi) $R^{3a}$ is H and $R^{3b}$ is H, $CH_3$, $CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$, $CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2$((4'-OH)-Ph), $CH_2SH$, or lower cycloalkyl; or (viii) $R^{3a}$ is $CH_3$, $-CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$, $CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2$((4'-OH)-Ph), $CH_2SH$, or lower cycloalkyl and $R^{3b}$ is H, where $R^{3'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{3''}$ is –OR' or $-N(R^{3'})_2$);

(d) $R^4$ is hydrogen, $C_{1-10}$ alkyl, $C_{1-10}$ alkyl optionally substituted with a lower alkyl, alkoxy, di(lower alkyl)-amino, or halogen, $C_{1-10}$ haloalkyl, $C_{3-10}$ cycloalkyl, cycloalkyl alkyl, cycloheteroalkyl, aminoacyl, aryl, such as phenyl, heteroaryl, such as, pyridinyl,substituted aryl, or substituted heteroaryl;

(e) $R^5$ is H, a lower alkyl, CN, vinyl, O-(lower alkyl), hydroxyl lower alkyl, i.e., $-(CH_2)_pOH$, where p is 1 -6, including hydroxyl methyl ($CH_2OH$), $CH_2F$, $N_3$, $CH_2CN$, $CH_2NH_2$, $CH_2NHCH_3$, $CH_2N(CH_3)_2$, alkyne (optionally substituted), or halogen, including F, Cl, Br, or I, with the provisos that when X is OH, base is cytosine and $R^6$ is H, $R^5$ cannot be $N_3$ and when X is OH, $R^6$ is $CH_3$ or $CH_2F$ and B is a purine base, $R^5$ cannot be H;

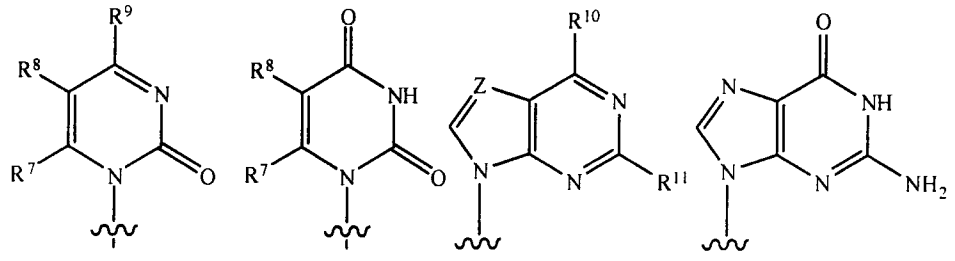
(f) $R^6$ is H, $CH_3$, $CH_2F$, $CHF_2$, $CF_3$, F, or CN;

(g) X is H, OH, F, OMe, halogen, $NH_2$, or $N_3$;

(h) Y is OH, H, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, vinyl, $N_3$, CN, Cl, Br, F, I, $NO_2$, OC(O)O($C_{1-4}$ alkyl), OC(O)O($C_{1-4}$ alkyl), OC(O)O($C_{2-4}$ alkynyl), OC(O)O($C_{2-4}$ alkenyl), $OC_{1-10}$ haloalkyl, O(aminoacyl), O($C_{1-10}$ acyl), O($C_{1-4}$ alkyl), O($C_{2-4}$ alkenyl), S($C_{1-4}$ acyl), S($C_{1-4}$ alkyl), S($C_{2-4}$ alkynyl), S($C_{2-4}$ alkenyl), SO($C_{1-4}$ acyl), SO($C_{1-4}$ alkyl), SO($C_{2-4}$ alkynyl), SO($C_{2-4}$ alkenyl),

$SO_2(C_{1-4}$ acyl), $SO_2(C_{1-4}$ alkyl), $SO_2(C_{2-4}$ alkynyl), $SO_2(C_{2-4}$ alkenyl), $OS(O)_2(C_{1-4}$ acyl), $OS(O)_2(C_{1-4}$ alkyl), $OS(O)_2(C_{2-4}$ alkenyl), $NH_2$, $NH(C_{1-4}$ alkyl), $NH(C_{2-4}$ alkenyl), $NH(C_{2-4}$ alkynyl), $NH(C_{1-4}$ acyl), $N(C_{1-4}$ alkyl$)_2$, $N(C_{1-18}$ acyl$)_2$, wherein alkyl, alkynyl, alkenyl and vinyl are optionally substituted by $N_3$, CN, one to three halogen (Cl, Br, F, I), $NO_2$, $C(O)O(C_{1-4}$ alkyl), $C(O)O(C_{1-4}$ alkyl), $C(O)O(C_{2-4}$ alkynyl), $C(O)O(C_{2-4}$ alkenyl), $O(C_{1-4}$ acyl), $O(C_{1-4}$ alkyl), $O(C_{2-4}$ alkenyl), $S(C_{1-4}$ acyl), $S(C_{1-4}$ alkyl), $S(C_{2-4}$ alkynyl), $S(C_{2-4}$ alkenyl), $SO(C_{1-4}$ acyl), $SO(C_{1-4}$ alkyl), $SO(C_{2-4}$ alkynyl), $SO(C_{2-4}$ alkenyl), $SO_2(C_{1-4}$ acyl), $SO_2(C_{1-4}$ alkyl), $SO_2(C_{2-4}$ alkynyl), $SO_2(C_{2-4}$ alkenyl), $OS(O)_2(C_{1-4}$ acyl), $OS(O)_2(C_{1-4}$ alkyl), $OS(O)_2(C_{2-4}$ alkenyl), $NH_2$, $NH(C_{1-4}$ alkyl), $NH(C_{2-4}$ alkenyl), $NH(C_{2-4}$ alkynyl), $NH(C_{1-4}$ acyl), $N(C_{1-4}$ alkyl$)_2$, $N(C_{1-4}$ acyl$)_2$;

the base is a naturally occurring or modified purine or pyrimidine base represented by the following structures:



**a** **b** **c** **d**

wherein

Z is N or $CR^{12}$;

$R^7$, $R^8$,$R^9$, $R^{10}$, and $R^{11}$are independently H, F, Cl, Br, I, OH, OR', SH, SR', $NH_2$, NHR', $NR'_2$, lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$, lower alkynyl of $C_2$-$C_6$ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', $CONR'_2$, $CH{=}CHCO_2H$, or $CH{=}CHCO_2R'$,

wherein R' is an optionally substituted alkyl , which includes, but is not limited to, an optionally substituted $C_{1-20}$ alkyl, an optionally substituted $C_{1-10}$ alkyl, an optionally substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted alkynyl of $C_2$-$C_6$, an optionally substituted lower alkenyl of $C_2$-$C_6$, or optionally substituted acyl, which includes but is not limited to C(O) alkyl, C(O)($C_{1-20}$ alkyl), C(O)($C_{1-10}$ alkyl), or C(O)(lower alkyl) or alternatively, in the instance of $NR'_2$, each R' comprise at least one C atom that are joined to form a heterocycle comprising at least two carbon atoms; and

$R^{12}$ is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', $NH_2$, NHR', $NR'_2$, $NO_2$ lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$ , lower alkynyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', $CONR'_2$, $CH{=}CHCO_2H$, or $CH{=}CHCO_2R'$; with the proviso that when base is represented by the structure c with $R^{11}$ being hydrogen, $R^{12}$ is not a: (i) $-C{\equiv}C-H$, (ii) $-C{=}CH_2$, or (iii) $-NO_2$.

2. A compound its stereoisomer, salt, hydrate, solvate, or crystalline form thereof selected from among

**5** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-alanyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester);

**6** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**7** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**8** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-alanyl phosphate (((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester);

**9** $N^4$-(*N,N*-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-*C*-methylcytidine;

**10** 2'-Deoxy-2'-fluoro-2'-C-methylcytidine 5'-(phenyl methoxy-alanyl phosphate (((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-

3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenyoxy-phosphorylamino}-propionic acid methyl ester);

**11** 2'-Deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(4-bromophenyl methoxy-valyl phosphate (2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**12** 2'-deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**13** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid ethyl ester;

**14** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid benzyl ester;

**15** {[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-acetic acid methyl ester;

**16** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**17** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid methyl ester;

**18** (S)-1-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphoryl}-pyrrolidine-2-carboxylic acid methyl ester;

**19** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**20** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**21** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid methyl ester;

**22** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**23** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**24** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid sec-butyl ester;

**25** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**26** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**27** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid ethyl ester;

**28** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**29** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**30** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**31** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid benzyl ester;

**32** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**33** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid isopropyl ester;

**34** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**35** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**36** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**37** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**38** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid pentyl ester;

**39** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**40** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**41** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**42** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid butyl ester;

**43** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid benzyl ester;

**44** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid methyl ester;

**45** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 4-fluoro-benzyl ester;

**46** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**47** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 3-methyl-butyl ester;

**48** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**49** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclohexyl ester;

**50** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**51** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**52** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**53** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**54** (S)-2-{(4-Bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**55** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**56** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-bromo-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**57** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid isopropyl ester;

**58** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclohexyl ester;

**59** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-butyric acid cyclohexyl ester;

**60** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4 R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-butyric acid isopropyl ester;

**61** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2-difluoro-ethyl ester;

**62** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2,2-trifluoro-1-trifluoromethyl-ethyl ester;

**63** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2-fluoro-1-fluoromethyl-ethyl ester;

**64** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclopropyl methyl ester;

**65** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclopentyl ester;

**66** (S)-2-{[(2R,3R,4R,5R)-5-(6-Amino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**67** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-hydroxy-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**68** (S)-2-{(R)-[(2R,3R,4R,5R)-5-(2,6-Diamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**69** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclopentylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**70** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-azetidin-1-yl-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**71** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-diethylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**72** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-propylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**73** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclobutylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**74** (S)-2-({(2R,3R,4R,5R)-5-[2-Amino-6-(4-methyl-piperazin-1-yl)-purin-9-y l]-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy}-phenoxy-p hosphorylamino)-propionic acid methyl ester;

**75** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(propylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**76** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclobutylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

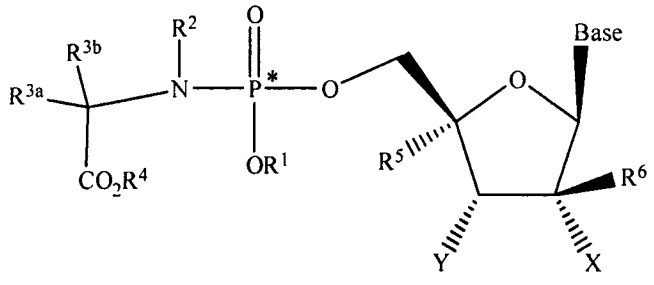
**77** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclopentylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**78** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(aziridin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**79** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(piperidin-1-yl)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate; and

**80** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate.

3. A composition for the treatment and/or prophylaxis of any of the viral agents disclosed herein said composition comprising a pharmaceutically acceptable medium selected from among an excipient, carrier, diluent, and equivalent medium and a compound, its stereoisomer, salt, hydrate, solvate, or crystalline form thereof, represented by formula I:




**I**

wherein

(a) $R^1$ is hydrogen, n-alkyl; branched alkyl; cycloalkyl; or aryl, which includes, but is not limited to, phenyl or naphthyl, where phenyl or naphthyl are optionally substituted with at least one of $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl,

$C_{1-6}$ alkoxy, F, Cl, Br, I, nitro, cyano, $C_{1-6}$ haloalkyl, $-N(R^{1'})_2$, $C_{1-6}$ acylamino, $-NHSO_2C_{1-6}$ alkyl, $-SO_2N(R^{1'})_2$, $COR^{1''}$, and $-SO_2C_{1-6}$ alkyl; ($R^{1'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{1''}$ is –OR' or $-N(R^{1'})_2$);

(b) $R^2$ is hydrogen, $C_{1-10}$ alkyl, $R^{3a}$ or $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms, $C(O)CR^{3a}R^{3b}NHR^1$, where n is 2 to 4 and $R^1$, $R^{3a}$, and $R^{3b}$;

(c) $R^{3a}$ and $R^{3b}$ are (i) independently selected from hydrogen, $C_{1-10}$ alkyl, cycloalkyl, $-(CH_2)_c(NR^{3'})_2$, $C_{1-6}$ hydroxyalkyl, $-CH_2SH$, $-(CH_2)_2S(O)_dMe$, $-(CH_2)_3NHC(=NH)NH_2$, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, $-(CH_2)_eCOR^{3''}$, aryl and aryl $C_{1-3}$ alkyl, said aryl groups optionally substituted with a group selected from hydroxyl, $C_{1-10}$ alkyl, $C_{1-6}$ alkoxy, halogen, nitro and cyano; (ii) $R^{3a}$ and $R^{3b}$ both are $C_{1-6}$ alkyl; (iii) $R^{3a}$ and $R^{3b}$ together are$(CH_2)_f$ so as to form a spiro ring; (iv) $R^{3a}$ is hydrogen and $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms (v) $R^{3b}$ is hydrogen and $R^{3a}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms, where c is 1 to 6, d is 0 to 2, e is 0 to 3, f is 2 to 5, n is 2 to 4, and where $R^{3'}$ is independently hydrogen or $C_{1-6}$ alkyl and $R^{3''}$ is -OR' or $-N(R^{3'})_2$); (vi) $R^{3a}$ is H and $R^{3b}$ is H, $CH_3$, $CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$, $CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2((4'-OH)-Ph)$, $CH_2SH$, or lower cycloalkyl; or (viii) $R^{3a}$ is $CH_3$, $-CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$, $CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2((4'-OH)-Ph)$, $CH_2SH$, or lower cycloalkyl and $R^{3b}$ is H, where $R^{3'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{3''}$ is –OR' or $-N(R^{3'})_2$);

(d) $R^4$ is hydrogen, $C_{1-10}$ alkyl, $C_{1-10}$ alkyl optionally substituted with a lower alkyl, alkoxy, di(lower alkyl)-amino, or halogen, $C_{1-10}$ haloalkyl, $C_{3-10}$

cycloalkyl, cycloalkyl alkyl, cycloheteroalkyl, aminoacyl, aryl, such as phenyl, heteroaryl, such as, pyridinyl, substituted aryl, or substituted heteroaryl;

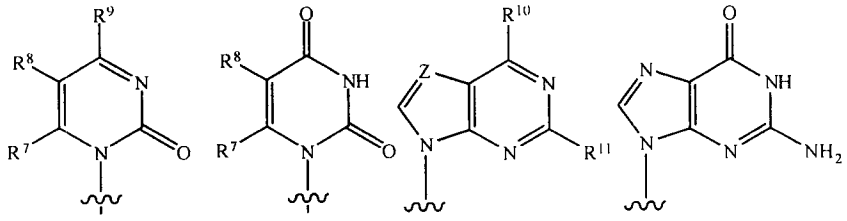
(e) $R^5$ is H, a lower alkyl, CN, vinyl, O-(lower alkyl), hydroxyl lower alkyl, i.e., $-(CH_2)_pOH$, where p is 1 -6, including hydroxyl methyl ($CH_2OH$), $CH_2F$, $N_3$, $CH_2CN$, $CH_2NH_2$, $CH_2NHCH_3$, $CH_2N(CH_3)_2$, alkyne (optionally substituted), or halogen, including F, Cl, Br, or I, with the provisos that when X is OH, base is cytosine and $R^6$ is H, $R^5$ cannot be $N_3$ and when X is OH, $R^6$ is $CH_3$ or $CH_2F$ and B is a purine base, $R^5$ cannot be H;

(f) $R^6$ is H, $CH_3$, $CH_2F$, $CHF_2$, $CF_3$, F, or CN;

(g) X is H, OH, F, OMe, halogen, $NH_2$, or $N_3$;

(h) Y is OH, H, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, vinyl, $N_3$, CN, Cl, Br, F, I, $NO_2$, OC(O)O($C_{1-4}$ alkyl), OC(O)O($C_{1-4}$ alkyl), OC(O)O($C_{2-4}$ alkynyl), OC(O)O($C_{2-4}$ alkenyl), $OC_{1-10}$ haloalkyl, O(aminoacyl), O($C_{1-10}$ acyl), O($C_{1-4}$ alkyl), O($C_{2-4}$ alkenyl), S($C_{1-4}$ acyl), S($C_{1-4}$ alkyl), S($C_{2-4}$ alkynyl), S($C_{2-4}$ alkenyl), SO($C_{1-4}$ acyl), SO($C_{1-4}$ alkyl), SO($C_{2-4}$ alkynyl), SO($C_{2-4}$ alkenyl), $SO_2$($C_{1-4}$ acyl), $SO_2$($C_{1-4}$ alkyl), $SO_2$($C_{2-4}$ alkynyl), $SO_2$($C_{2-4}$ alkenyl), $OS(O)_2$($C_{1-4}$ acyl), $OS(O)_2$($C_{1-4}$ alkyl), $OS(O)_2$($C_{2-4}$ alkenyl), $NH_2$, NH($C_{1-4}$ alkyl), NH($C_{2-4}$ alkenyl), NH($C_{2-4}$ alkynyl), NH($C_{1-4}$ acyl), N($C_{1-4}$ alkyl)$_2$, N($C_{1-18}$ acyl)$_2$, wherein alkyl, alkynyl, alkenyl and vinyl are optionally substituted by $N_3$, CN, one to three halogen (Cl, Br, F, I), $NO_2$, C(O)O($C_{1-4}$ alkyl), C(O)O($C_{1-4}$ alkyl), C(O)O($C_{2-4}$ alkynyl), C(O)O($C_{2-4}$ alkenyl), O($C_{1-4}$ acyl), O($C_{1-4}$ alkyl), O($C_{2-4}$ alkenyl), S($C_{1-4}$ acyl), S($C_{1-4}$ alkyl), S($C_{2-4}$ alkynyl), S($C_{2-4}$ alkenyl), SO($C_{1-4}$ acyl), SO($C_{1-4}$ alkyl), SO($C_{2-4}$ alkynyl), SO($C_{2-4}$ alkenyl), $SO_2$($C_{1-4}$ acyl), $SO_2$($C_{1-4}$ alkyl), $SO_2$($C_{2-4}$ alkynyl), $SO_2$($C_{2-4}$ alkenyl), $OS(O)_2$($C_{1-4}$ acyl), $OS(O)_2$($C_{1-4}$ alkyl), $OS(O)_2$($C_{2-4}$ alkenyl), $NH_2$, NH($C_{1-4}$ alkyl), NH($C_{2-4}$ alkenyl), NH($C_{2-4}$ alkynyl), NH($C_{1-4}$ acyl), N($C_{1-4}$ alkyl)$_2$, N($C_{1-4}$ acyl)$_2$;

the base is a naturally occurring or modified purine or pyrimidine base represented by the following structures:



**a** **b** **c** **d**

wherein

Z is N or $CR^{12}$;

$R^7$, $R^8$,$R^9$, $R^{10}$, and $R^{11}$are independently H, F, Cl, Br, I, OH, OR', SH, SR', $NH_2$, NHR', $NR'_2$, lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$, lower alkynyl of $C_2$-$C_6$ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', $CONR'_2$, $CH{=}CHCO_2H$, or $CH{=}CHCO_2R'$,

wherein R' is an optionally substituted alkyl , which includes, but is not limited to, an optionally substituted $C_{1-20}$ alkyl, an optionally substituted $C_{1-10}$ alkyl, an optionally substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted alkynyl of $C_2$-$C_6$, an optionally substituted lower alkenyl of $C_2$-$C_6$, or optionally substituted acyl, which includes but is not limited to C(O) alkyl, C(O)($C_{1-20}$ alkyl), C(O)($C_{1-10}$ alkyl), or C(O)(lower alkyl) or alternatively, in the instance of $NR'_2$, each R' comprise at least one C atom that are joined to form a heterocycle comprising at least two carbon atoms; and

$R^{12}$ is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', $NH_2$, NHR', $NR'_2$, $NO_2$ lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$ , lower alkynyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', $CONR'_2$, $CH{=}CHCO_2H$, or $CH{=}CHCO_2R'$; with the proviso that when base is represented by the structure c with $R^{11}$ being hydrogen, $R^{12}$ is not a: (i) –C≡C–H, (ii) $-C{=}CH_2$, or (iii) $-NO_2$.

4. A composition for the treatment and/or prophylaxis of any of the viral agents disclosed herein said composition comprising a pharmaceutically acceptable medium selected from among an excipient, carrier, diluent, and equivalent medium and a compound, its stereoisomer, salt, hydrate, solvate, or crystalline form thereof, selected from among

**5** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-alanyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester);

**6** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**7** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**8** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-alanyl phosphate (((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester);

**9** $N^4$-(*N,N*-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-*C*-methylcytidine;

**10** 2'-Deoxy-2'-fluoro-2'-C-methylcytidine 5'-(phenyl methoxy-alanyl phosphate (((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenyoxy-phosphorylamino}-propionic acid methyl ester);

**11** 2'-Deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(4-bromophenyl methoxy-valyl phosphate (2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**12** 2'-deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**13** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid ethyl ester;

**14** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid benzyl ester;

**15** {[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-acetic acid methyl ester;

**16** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**17** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid methyl ester;

**18** (S)-1-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphoryl}-pyrrolidine-2-carboxylic acid methyl ester;

**19** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**20** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**21** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid methyl ester;

**22** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**23** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**24** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid sec-butyl ester;

**25** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**26** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**27** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid ethyl ester;

**28** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**29** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**30** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**31** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid benzyl ester;

**32** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**33** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid isopropyl ester;

**34** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**35** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**36** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**37** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**38** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid pentyl ester;

**39** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**40** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**41** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**42** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid butyl ester;

**43** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid benzyl ester;

**44** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid methyl ester;

**45** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 4-fluoro-benzyl ester;

**46** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**47** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 3-methyl-butyl ester;

**48** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**49** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclohexyl ester;

**50** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**51** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**52** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**53** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**54** (S)-2-{(4-Bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**55** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**56** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-bromo-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**57** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid isopropyl ester;

**58** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclohexyl ester;

**59** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-butyric acid cyclohexyl ester;

**60** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4 R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-butyric acid isopropyl ester;

**61** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2-difluoro-ethyl ester;

**62** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2,2-trifluoro-1-trifluoromethyl-ethyl ester;

**63** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2-fluoro-1-fluoromethyl-ethyl ester;

**64** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclopropyl methyl ester;

**65** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclopentyl ester;

**66** (S)-2-{[(2R,3R,4R,5R)-5-(6-Amino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**67** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-hydroxy-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**68** (S)-2-{(R)-[(2R,3R,4R,5R)-5-(2,6-Diamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**69** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclopentylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**70** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-azetidin-1-yl-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**71** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-diethylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**72** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-propylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**73** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclobutylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**74** (S)-2-({(2R,3R,4R,5R)-5-[2-Amino-6-(4-methyl-piperazin-1-yl)-purin-9-y l]-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy}-phenoxy-p hosphorylamino)-propionic acid methyl ester;

**75** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(propylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**76** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclobutylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**77** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclopentylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

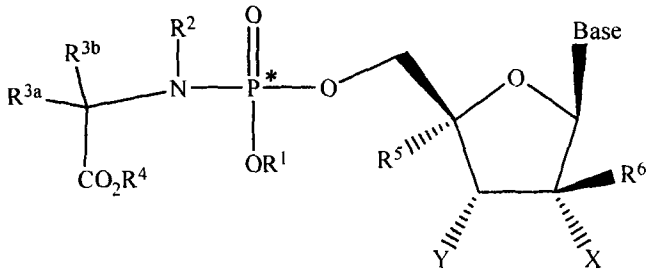
**78** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(aziridin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**79** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(piperidin-1-yl)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate; and

**80** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate.

5. The compound represented by formula I adapted for the treatment of any condition the result of an infection by hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus.

wherein the compound, its stereoisomer, salt, hydrate, solvate, or crystalline form thereof, are represented by formula I:




I

wherein

(a) $R^1$ is hydrogen, n-alkyl; branched alkyl; cycloalkyl; or aryl, which includes, but is not limited to, phenyl or naphthyl, where phenyl or naphthyl are optionally substituted with at least one of $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{1-6}$ alkoxy, F, Cl, Br, I, nitro, cyano, $C_{1-6}$ haloalkyl, $-N(R^{1'})_2$, $C_{1-6}$ acylamino, $-NHSO_2C_{1-6}$ alkyl, $-SO_2N(R^{1'})_2$, $COR^{1''}$, and $-SO_2C_{1-6}$ alkyl; ($R^{1'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{1''}$ is –OR' or $-N(R^{1'})_2$);

(b) $R^2$ is hydrogen, $C_{1-10}$ alkyl, $R^{3a}$ or $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms, $C(O)CR^{3a}R^{3b}NHR^1$, where n is 2 to 4 and $R^1$, $R^{3a}$, and $R^{3b}$;

(c) $R^{3a}$ and $R^{3b}$ are (i) independently selected from hydrogen, $C_{1-10}$ alkyl, cycloalkyl, $-(CH_2)_c(NR^{3'})_2$, $C_{1-6}$ hydroxyalkyl, $-CH_2SH$, $-(CH_2)_2S(O)_dMe$, $-(CH_2)_3NHC(=NH)NH_2$, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, -

$(CH_2)_eCOR^{3''}$, aryl and aryl $C_{1-3}$ alkyl, said aryl groups optionally substituted with a group selected from hydroxyl, $C_{1-10}$ alkyl, $C_{1-6}$ alkoxy, halogen, nitro and cyano; (ii) $R^{3a}$ and $R^{3b}$ both are $C_{1-6}$ alkyl; (iii) $R^{3a}$ and $R^{3b}$ together are$(CH_2)_f$ so as to form a spiro ring; (iv) $R^{3a}$ is hydrogen and $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms (v) $R^{3b}$ is hydrogen and $R^{3a}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms, where c is 1 to 6, d is 0 to 2, e is 0 to 3, f is 2 to 5, n is 2 to 4, and where $R^{3'}$ is independently hydrogen or $C_{1-6}$ alkyl and $R^{3''}$ is -OR' or $-N(R^{3'})_2$); (vi) $R^{3a}$ is H and $R^{3b}$ is H, $CH_3$, $CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$, $CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2((4'-OH)-Ph)$, $CH_2SH$, or lower cycloalkyl; or (viii) $R^{3a}$ is $CH_3$, $-CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$, $CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2((4'-OH)-Ph)$, $CH_2SH$, or lower cycloalkyl and $R^{3b}$ is H, where $R^{3'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{3''}$ is –OR' or $-N(R^{3'})_2$);

(d) $R^4$ is hydrogen, $C_{1-10}$ alkyl, $C_{1-10}$ alkyl optionally substituted with a lower alkyl, alkoxy, di(lower alkyl)-amino, or halogen, $C_{1-10}$ haloalkyl, $C_{3-10}$ cycloalkyl, cycloalkyl alkyl, cycloheteroalkyl, aminoacyl, aryl, such as phenyl, heteroaryl, such as, pyridinyl, substituted aryl, or substituted heteroaryl;

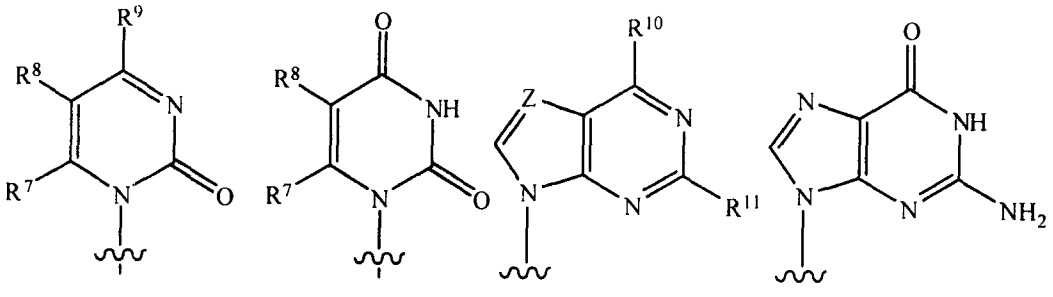
(e) $R^5$ is H, a lower alkyl, CN, vinyl, O-(lower alkyl), hydroxyl lower alkyl, i.e., $-(CH_2)_pOH$, where p is 1 -6, including hydroxyl methyl ($CH_2OH$), $CH_2F$, $N_3$, $CH_2CN$, $CH_2NH_2$, $CH_2NHCH_3$, $CH_2N(CH_3)_2$, alkyne (optionally substituted), or halogen, including F, Cl, Br, or I, with the provisos that when X is OH, base is cytosine and $R^6$ is H, $R^5$ cannot be $N_3$ and when X is OH, $R^6$ is $CH_3$ or $CH_2F$ and B is a purine base, $R^5$ cannot be H;

(f) $R^6$ is H, $CH_3$, $CH_2F$, $CHF_2$, $CF_3$, F, or CN;

(g) X is H, OH, F, OMe, halogen, $NH_2$, or $N_3$;

(h) Y is OH, H, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, vinyl, $N_3$, CN, Cl, Br, F, I, $NO_2$, $OC(O)O(C_{1-4}$ alkyl), $OC(O)O(C_{1-4}$ alkyl), $OC(O)O(C_{2-4}$ alkynyl), $OC(O)O(C_{2-4}$ alkenyl), $OC_{1-10}$ haloalkyl, O(aminoacyl), $O(C_{1-10}$ acyl), $O(C_{1-4}$ alkyl), $O(C_{2-4}$ alkenyl), $S(C_{1-4}$ acyl), $S(C_{1-4}$ alkyl), $S(C_{2-4}$ alkynyl), $S(C_{2-4}$ alkenyl), $SO(C_{1-4}$ acyl), $SO(C_{1-4}$ alkyl), $SO(C_{2-4}$ alkynyl), $SO(C_{2-4}$ alkenyl), $SO_2(C_{1-4}$ acyl), $SO_2(C_{1-4}$ alkyl), $SO_2(C_{2-4}$ alkynyl), $SO_2(C_{2-4}$ alkenyl), $OS(O)_2(C_{1-4}$ acyl), $OS(O)_2(C_{1-4}$ alkyl), $OS(O)_2(C_{2-4}$ alkenyl), $NH_2$, $NH(C_{1-4}$ alkyl), $NH(C_{2-4}$ alkenyl), $NH(C_{2-4}$ alkynyl), $NH(C_{1-4}$ acyl), $N(C_{1-4}$ alkyl$)_2$, $N(C_{1-18}$ acyl$)_2$, wherein alkyl, alkynyl, alkenyl and vinyl are optionally substituted by $N_3$, CN, one to three halogen (Cl, Br, F, I), $NO_2$, $C(O)O(C_{1-4}$ alkyl), $C(O)O(C_{1-4}$ alkyl), $C(O)O(C_{2-4}$ alkynyl), $C(O)O(C_{2-4}$ alkenyl), $O(C_{1-4}$ acyl), $O(C_{1-4}$ alkyl), $O(C_{2-4}$ alkenyl), $S(C_{1-4}$ acyl), $S(C_{1-4}$ alkyl), $S(C_{2-4}$ alkynyl), $S(C_{2-4}$ alkenyl), $SO(C_{1-4}$ acyl), $SO(C_{1-4}$ alkyl), $SO(C_{2-4}$ alkynyl), $SO(C_{2-4}$ alkenyl), $SO_2(C_{1-4}$ acyl), $SO_2(C_{1-4}$ alkyl), $SO_2(C_{2-4}$ alkynyl), $SO_2(C_{2-4}$ alkenyl), $OS(O)_2(C_{1-4}$ acyl), $OS(O)_2(C_{1-4}$ alkyl), $OS(O)_2(C_{2-4}$ alkenyl), $NH_2$, $NH(C_{1-4}$ alkyl), $NH(C_{2-4}$ alkenyl), $NH(C_{2-4}$ alkynyl), $NH(C_{1-4}$ acyl), $N(C_{1-4}$ alkyl$)_2$, $N(C_{1-4}$ acyl$)_2$;

the base is a naturally occurring or modified purine or pyrimidine base represented by the following structures:



**a** **b** **c** **d**

wherein

Z is N or $CR^{12}$;

$R^7$, $R^8$,$R^9$, $R^{10}$, and $R^{11}$are independently H, F, Cl, Br, I, OH, OR', SH, SR', $NH_2$, NHR', $NR'_2$, lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$, lower alkynyl of $C_2$-$C_6$ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', $CONR'_2$, $CH{=}CHCO_2H$, or $CH{=}CHCO_2R'$,

wherein R' is an optionally substituted alkyl , which includes, but is not limited to, an optionally substituted $C_{1-20}$ alkyl, an optionally substituted $C_{1-10}$ alkyl, an optionally substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted alkynyl of $C_2$-$C_6$, an optionally substituted lower alkenyl of $C_2$-$C_6$, or optionally substituted acyl, which includes but is not limited to C(O) alkyl, C(O)($C_{1-20}$ alkyl), C(O)($C_{1-10}$ alkyl), or C(O)(lower alkyl) or alternatively, in the instance of $NR'_2$, each R' comprise at least one C atom that are joined to form a heterocycle comprising at least two carbon atoms; and

$R^{12}$ is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', $NH_2$, NHR', $NR'_2$, $NO_2$ lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$ , lower alkynyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', $CONR'_2$, $CH{=}CHCO_2H$, or $CH{=}CHCO_2R'$; with the proviso that when base is represented by the structure c with $R^{11}$ being hydrogen, $R^{12}$ is not a: (i) –C≡C–H, (ii) $-C{=}CH_2$, or (iii) $-NO_2$.

6. A compound, its stereoisomer, salt, hydrate, solvate, or crystalline form thereof, selected from among

**5** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-alanyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester);

**6** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**7** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**8** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-alanyl phosphate (((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester);

**9** $N^4$-(*N,N*-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-*C*-methylcytidine;

**10** 2'-Deoxy-2'-fluoro-2'-C-methylcytidine 5'-(phenyl methoxy-alanyl phosphate (((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenyoxy-phosphorylamino}-propionic acid methyl ester);

**11** 2'-Deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(4-bromophenyl methoxy-valyl phosphate (2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**12** 2'-deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**13** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid ethyl ester;

**14** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid benzyl ester;

**15** {[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-acetic acid methyl ester;

**16** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**17** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid methyl ester;

**18** (S)-1-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphoryl}-pyrrolidine-2-carboxylic acid methyl ester;

**19** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**20** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**21** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid methyl ester;

**22** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**23** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**24** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid sec-butyl ester;

**25** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**26** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**27** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid ethyl ester;

**28** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**29** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**30** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**31** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid benzyl ester;

**32** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**33** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid isopropyl ester;

**34** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**35** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**36** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**37** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**38** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid pentyl ester;

**39** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**40** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**41** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**42** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid butyl ester;

**43** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid benzyl ester;

**44** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid methyl ester;

**45** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 4-fluoro-benzyl ester;

**46** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**47** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 3-methyl-butyl ester;

**48** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**49** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclohexyl ester;

**50** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**51** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**52** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**53** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**54** (S)-2-{(4-Bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**55** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**56** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-bromo-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**57** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid isopropyl ester;

**58** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclohexyl ester;

**59** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-butyric acid cyclohexyl ester;

**60** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4 R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-butyric acid isopropyl ester;

**61** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2-difluoro-ethyl ester;

**62** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2,2-trifluoro-1-trifluoromethyl-ethyl ester;

**63** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2-fluoro-1-fluoromethyl-ethyl ester;

**64** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclopropyl methyl ester;

**65** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclopentyl ester;

**66** (S)-2-{[(2R,3R,4R,5R)-5-(6-Amino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**67** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-hydroxy-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**68** (S)-2-{(R)-[(2R,3R,4R,5R)-5-(2,6-Diamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**69** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclopentylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**70** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-azetidin-1-yl-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**71** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-diethylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**72** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-propylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**73** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclobutylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**74** (S)-2-({(2R,3R,4R,5R)-5-[2-Amino-6-(4-methyl-piperazin-1-yl)-purin-9-y l]-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy}-phenoxy-p hosphorylamino)-propionic acid methyl ester;

**75** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(propylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**76** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclobutylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**77** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclopentylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

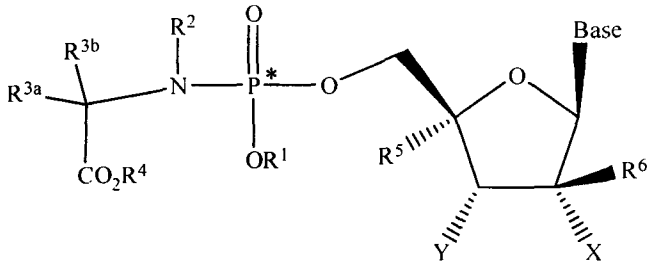
**78** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(aziridin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**79** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(piperidin-1-yl)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate; and

**80** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate

adapted for the treatment of any condition the result of an infection by hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus.

7. A process for preparing a compound, its stereoisomer, salt, hydrate, solvate, or crystalline form thereof, represented by formula I:




**I**

wherein

(a) $R^1$ is hydrogen, n-alkyl; branched alkyl; cycloalkyl; or aryl, which includes, but is not limited to, phenyl or naphthyl, where phenyl or naphthyl are optionally substituted with at least one of $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{1-6}$ alkoxy, F, Cl, Br, I, nitro, cyano, $C_{1-6}$ haloalkyl, $-N(R^{1'})_2$, $C_{1-6}$ acylamino, $-NHSO_2C_{1-6}$ alkyl, $-SO_2N(R^{1'})_2$, $COR^{1''}$, and $-SO_2C_{1-6}$ alkyl; ($R^{1'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{1''}$ is –OR' or $-N(R^{1'})_2$);

(b) $R^2$ is hydrogen, $C_{1-10}$ alkyl, $R^{3a}$ or $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms, $C(O)CR^{3a}R^{3b}NHR^1$, where n is 2 to 4 and $R^1$, $R^{3a}$, and $R^{3b}$;

(c) $R^{3a}$ and $R^{3b}$ are (i) independently selected from hydrogen, $C_{1-10}$ alkyl, cycloalkyl, $-(CH_2)_c(NR^{3'})_2$, $C_{1-6}$ hydroxyalkyl, $-CH_2SH$, $-(CH_2)_2S(O)_dMe$, $-(CH_2)_3NHC(=NH)NH_2$, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, $-(CH_2)_eCOR^{3''}$, aryl and aryl $C_{1-3}$ alkyl, said aryl groups optionally substituted with a group selected from hydroxyl, $C_{1-10}$ alkyl, $C_{1-6}$ alkoxy, halogen, nitro and cyano; (ii) $R^{3a}$ and $R^{3b}$ both are $C_{1-6}$ alkyl; (iii) $R^{3a}$ and $R^{3b}$ together are$(CH_2)_f$ so as to form a spiro ring; (iv) $R^{3a}$ is hydrogen and $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms (v) $R^{3b}$ is hydrogen and $R^{3a}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms, where c is 1 to 6, d is 0 to 2, e is 0 to 3, f is 2 to 5, n is 2 to 4, and where $R^{3'}$ is independently hydrogen or $C_{1-6}$ alkyl and $R^{3''}$ is -OR' or $-N(R^{3'})_2$); (vi) $R^{3a}$ is H and $R^{3b}$ is H, $CH_3$, $CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$,

$CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2$((4'-OH)-Ph), $CH_2SH$, or lower cycloalkyl; or (viii) $R^{3a}$ is $CH_3$, $-CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$, $CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2$((4'-OH)-Ph), $CH_2SH$, or lower cycloalkyl and $R^{3b}$ is H, where $R^{3'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{3''}$ is –OR' or $-N(R^{3'})_2$);

(d) $R^4$ is hydrogen, $C_{1-10}$ alkyl, $C_{1-10}$ alkyl optionally substituted with a lower alkyl, alkoxy, di(lower alkyl)-amino, or halogen, $C_{1-10}$ haloalkyl, $C_{3-10}$ cycloalkyl, cycloalkyl alkyl, cycloheteroalkyl, aminoacyl, aryl, such as phenyl, heteroaryl, such as, pyridinyl, substituted aryl, or substituted heteroaryl;

(e) $R^5$ is H, a lower alkyl, CN, vinyl, O-(lower alkyl), hydroxyl lower alkyl, i.e., $-(CH_2)_pOH$, where p is 1 -6, including hydroxyl methyl ($CH_2OH$), $CH_2F$, $N_3$, $CH_2CN$, $CH_2NH_2$, $CH_2NHCH_3$, $CH_2N(CH_3)_2$, alkyne (optionally substituted), or halogen, including F, Cl, Br, or I, with the provisos that when X is OH, base is cytosine and $R^6$ is H, $R^5$ cannot be $N_3$ and when X is OH, $R^6$ is $CH_3$ or $CH_2F$ and B is a purine base, $R^5$ cannot be H;

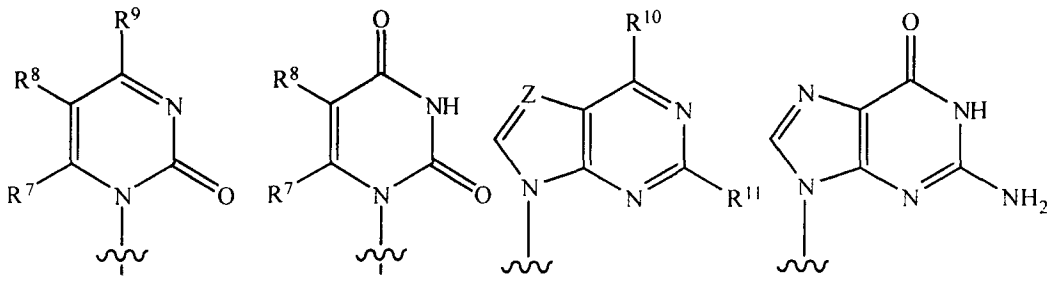
(f) $R^6$ is H, $CH_3$, $CH_2F$, $CHF_2$, $CF_3$, F, or CN;

(g) X is H, OH, F, OMe, halogen, $NH_2$, or $N_3$;

(h) Y is OH, H, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, vinyl, $N_3$, CN, Cl, Br, F, I, $NO_2$, $OC(O)O(C_{1-4}$ alkyl), $OC(O)O(C_{1-4}$ alkyl), $OC(O)O(C_{2-4}$ alkynyl), $OC(O)O(C_{2-4}$ alkenyl), $OC_{1-10}$ haloalkyl, O(aminoacyl), $O(C_{1-10}$ acyl), $O(C_{1-4}$ alkyl), $O(C_{2-4}$ alkenyl), $S(C_{1-4}$ acyl), $S(C_{1-4}$ alkyl), $S(C_{2-4}$ alkynyl), $S(C_{2-4}$ alkenyl), $SO(C_{1-4}$ acyl), $SO(C_{1-4}$ alkyl), $SO(C_{2-4}$ alkynyl), $SO(C_{2-4}$ alkenyl), $SO_2(C_{1-4}$ acyl), $SO_2(C_{1-4}$ alkyl), $SO_2(C_{2-4}$ alkynyl), $SO_2(C_{2-4}$ alkenyl), $OS(O)_2(C_{1-4}$ acyl), $OS(O)_2(C_{1-4}$ alkyl), $OS(O)_2(C_{2-4}$ alkenyl), $NH_2$, $NH(C_{1-4}$ alkyl), $NH(C_{2-4}$ alkenyl), $NH(C_{2-4}$ alkynyl), $NH(C_{1-4}$ acyl), $N(C_{1-4}$ alkyl$)_2$, $N(C_{1-18}$ acyl$)_2$, wherein alkyl, alkynyl, alkenyl and vinyl are optionally substituted by $N_3$, CN,

one to three halogen (Cl, Br, F, I), $NO_2$, $C(O)O(C_{1-4}$ alkyl), $C(O)O(C_{1-4}$ alkyl), $C(O)O(C_{2-4}$ alkynyl), $C(O)O(C_{2-4}$ alkenyl), $O(C_{1-4}$ acyl), $O(C_{1-4}$ alkyl), $O(C_{2-4}$ alkenyl), $S(C_{1-4}$ acyl), $S(C_{1-4}$ alkyl), $S(C_{2-4}$ alkynyl), $S(C_{2-4}$ alkenyl), $SO(C_{1-4}$ acyl), $SO(C_{1-4}$ alkyl), $SO(C_{2-4}$ alkynyl), $SO(C_{2-4}$ alkenyl), $SO_2(C_{1-4}$ acyl), $SO_2(C_{1-4}$ alkyl), $SO_2(C_{2-4}$ alkynyl), $SO_2(C_{2-4}$ alkenyl), $OS(O)_2(C_{1-4}$ acyl), $OS(O)_2(C_{1-4}$ alkyl), $OS(O)_2(C_{2-4}$ alkenyl), $NH_2$, $NH(C_{1-4}$ alkyl), $NH(C_{2-4}$ alkenyl), $NH(C_{2-4}$ alkynyl), $NH(C_{1-4}$ acyl), $N(C_{1-4}$ alkyl$)_2$, $N(C_{1-4}$ acyl$)_2$;

the base is a naturally occurring or modified purine or pyrimidine base represented by the following structures:



**a** **b** **c** **d**

wherein

Z is N or $CR^{12}$;

$R^7$, $R^8$,$R^9$, $R^{10}$, and $R^{11}$are independently H, F, Cl, Br, I, OH, OR', SH, SR', $NH_2$, NHR', $NR'_2$, lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$, lower alkynyl of $C_2$-$C_6$ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', $CONR'_2$, $CH{=}CHCO_2H$, or $CH{=}CHCO_2R'$,

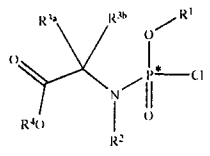
wherein R' is an optionally substituted alkyl , which includes, but is not limited to, an optionally substituted $C_{1-20}$ alkyl, an optionally substituted $C_{1-10}$

alkyl, an optionally substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted alkynyl of $C_2$-$C_6$, an optionally substituted lower alkenyl of $C_2$-$C_6$, or optionally substituted acyl, which includes but is not limited to C(O) alkyl, C(O)($C_{1-20}$ alkyl), C(O)($C_{1-10}$ alkyl), or C(O)(lower alkyl) or alternatively, in the instance of $NR'_2$, each R' comprise at least one C atom that are joined to form a heterocycle comprising at least two carbon atoms; and

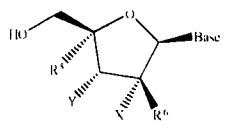
$R^{12}$ is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', $NH_2$, NHR', $NR'_2$, $NO_2$ lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$ , lower alkynyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', $CONR'_2$, $CH{=}CHCO_2H$, or $CH{=}CHCO_2R'$; with the proviso that when base is represented by the structure c with $R^{11}$ being hydrogen, $R^{12}$ is not a: (i) $-C{\equiv}C-H$, (ii) $-C{=}CH_2$, or (iii) $-NO_2$;

said process comprising:

reacting a substituted phosphochloridate compound **4** with a nucleoside analog **5**



**4**



**5** .

8. A process for preparing a compound, its stereoisomer, salt, hydrate, solvate, or crystalline form thereof, selected from among

**5** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-alanyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester);

**6** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**7** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-

dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**8** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-alanyl phosphate (((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester);

**9** $N^4$-(*N,N*-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-*C*-methylcytidine;

**10** 2'-Deoxy-2'-fluoro-2'-C-methylcytidine 5'-(phenyl methoxy-alanyl phosphate (((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenyoxy-phosphorylamino}-propionic acid methyl ester);

**11** 2'-Deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(4-bromophenyl methoxy-valyl phosphate (2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**12** 2'-deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**13** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid ethyl ester;

**14** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid benzyl ester;

**15** {[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-acetic acid methyl ester;

**16** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**17** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid methyl ester;

**18** (S)-1-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphoryl}-pyrrolidine-2-carboxylic acid methyl ester;

**19** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**20** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**21** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid methyl ester;

**22** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**23** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**24** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid sec-butyl ester;

**25** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**26** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**27** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid ethyl ester;

**28** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**29** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**30** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**31** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid benzyl ester;

**32** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**33** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid isopropyl ester;

**34** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**35** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**36** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**37** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**38** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid pentyl ester;

**39** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**40** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**41** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**42** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid butyl ester;

**43** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid benzyl ester;

**44** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid methyl ester;

**45** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 4-fluoro-benzyl ester;

**46** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**47** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 3-methyl-butyl ester;

**48** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**49** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclohexyl ester;

**50** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**51** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**52** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**53** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**54** (S)-2-{(4-Bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**55** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**56** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-bromo-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**57** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid isopropyl ester;

**58** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclohexyl ester;

**59** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-butyric acid cyclohexyl ester;

**60** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4 R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-butyric acid isopropyl ester;

**61** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2-difluoro-ethyl ester;

**62** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2,2-trifluoro-1-trifluoromethyl-ethyl ester;

**63** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2-fluoro-1-fluoromethyl-ethyl ester;

**64** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclopropyl methyl ester;

**65** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclopentyl ester;

**66** (S)-2-{[(2R,3R,4R,5R)-5-(6-Amino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**67** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-hydroxy-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**68** (S)-2-{(R)-[(2R,3R,4R,5R)-5-(2,6-Diamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**69** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclopentylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**70** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-azetidin-1-yl-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**71** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-diethylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**72** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-propylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**73** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclobutylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**74** (S)-2-({(2R,3R,4R,5R)-5-[2-Amino-6-(4-methyl-piperazin-1-yl)-purin-9-y l]-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy}-phenoxy-p hosphorylamino)-propionic acid methyl ester;

**75** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(propylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**76** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclobutylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**77** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclopentylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

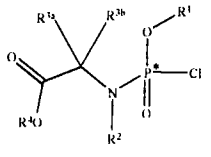
**78** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(aziridin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**79** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(piperidin-1-yl)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate; and

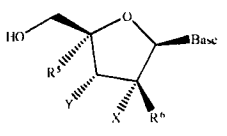
**80** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate

said process comprising:

reacting a substituted phosphochloridate compound **4** with a nucleoside analog **5**



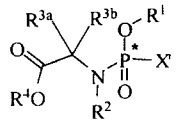
**4**



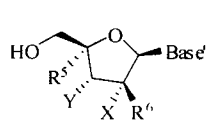
**5**

9. A product its stereoisomer, salt, hydrate, solvate or crystalline form thereof, prepared a process comprising:

reacting a substituted phosphochloridate compound **4** with a nucleoside analog **5**



**4**



**5**

wherein

(a) $R^1$ is hydrogen, n-alkyl; branched alkyl; cycloalkyl; or aryl, which includes, but is not limited to, phenyl or naphthyl, where phenyl or naphthyl are optionally substituted with at least one of $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{1-6}$ alkoxy, F, Cl, Br, I, nitro, cyano, $C_{1-6}$ haloalkyl, $-N(R^{1'})_2$, $C_{1-6}$ acylamino, $-NHSO_2C_{1-6}$ alkyl, $-SO_2N(R^{1'})_2$, $COR^{1''}$, and $-SO_2C_{1-6}$ alkyl; ($R^{1'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{1''}$ is –OR' or $-N(R^{1'})_2$);

(b) $R^2$ is hydrogen, $C_{1-10}$ alkyl, $R^{3a}$ or $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms, $C(O)CR^{3a}R^{3b}NHR^1$, where n is 2 to 4 and $R^1$, $R^{3a}$, and $R^{3b}$;

(c) $R^{3a}$ and $R^{3b}$ are (i) independently selected from hydrogen, $C_{1-10}$ alkyl, cycloalkyl, $-(CH_2)_c(NR^{3'})_2$, $C_{1-6}$ hydroxyalkyl, $-CH_2SH$, $-(CH_2)_2S(O)_dMe$, $-(CH_2)_3NHC(=NH)NH_2$, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, $-(CH_2)_eCOR^{3''}$, aryl and aryl $C_{1-3}$ alkyl, said aryl groups optionally substituted with a group selected from hydroxyl, $C_{1-10}$ alkyl, $C_{1-6}$ alkoxy, halogen, nitro and cyano; (ii) $R^{3a}$ and $R^{3b}$ both are $C_{1-6}$ alkyl; (iii) $R^{3a}$ and $R^{3b}$ together are$(CH_2)_f$ so as to form a spiro ring; (iv) $R^{3a}$ is hydrogen and $R^{3b}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms (v) $R^{3b}$ is hydrogen and $R^{3a}$ and $R^2$ together are $(CH_2)_n$ so as to form a cyclic ring that includes the adjoining N and C atoms, where c is 1 to 6, d is 0 to 2, e is 0 to 3, f is 2 to 5, n is 2 to 4, and where $R^{3'}$ is independently hydrogen or $C_{1-6}$ alkyl and

$R^{3''}$ is -OR' or $-N(R^{3'})_2$); (vi) $R^{3a}$ is H and $R^{3b}$ is H, $CH_3$, $CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$, $CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2$((4'-OH)-Ph), $CH_2SH$, or lower cycloalkyl; or (viii) $R^{3a}$ is $CH_3$, $-CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $CH_2Ph$, $CH_2$-indol-3-yl, $-CH_2CH_2SCH_3$, $CH_2CO_2H$, $CH_2C(O)NH_2$, $CH_2CH_2COOH$, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $CH_2$-imidazol-4-yl, $CH_2OH$, $CH(OH)CH_3$, $CH_2$((4'-OH)-Ph), $CH_2SH$, or lower cycloalkyl and $R^{3b}$ is H, where $R^{3'}$ is independently hydrogen or alkyl, which includes, but is not limited to, $C_{1-20}$ alkyl, $C_{1-10}$ alkyl, or $C_{1-6}$ alkyl, $R^{3''}$ is –OR' or $-N(R^{3'})_2$);

(d) $R^4$ is hydrogen, $C_{1-10}$ alkyl, $C_{1-10}$ alkyl optionally substituted with a lower alkyl, alkoxy, di(lower alkyl)-amino, or halogen, $C_{1-10}$ haloalkyl, $C_{3-10}$ cycloalkyl, cycloalkyl alkyl, cycloheteroalkyl, aminoacyl, aryl, such as phenyl, heteroaryl, such as, pyridinyl, substituted aryl, or substituted heteroaryl;

(e) $R^5$ is H, a lower alkyl, CN, vinyl, O-(lower alkyl), hydroxyl lower alkyl, i.e., $-(CH_2)_pOH$, where p is 1 -6, including hydroxyl methyl ($CH_2OH$), $CH_2F$, $N_3$, $CH_2CN$, $CH_2NH_2$, $CH_2NHCH_3$, $CH_2N(CH_3)_2$, alkyne (optionally substituted), or halogen, including F, Cl, Br, or I, with the provisos that when X is OH, base is cytosine and $R^6$ is H, $R^5$ cannot be $N_3$ and when X is OH, $R^6$ is $CH_3$ or $CH_2F$ and B is a purine base, $R^5$ cannot be H;

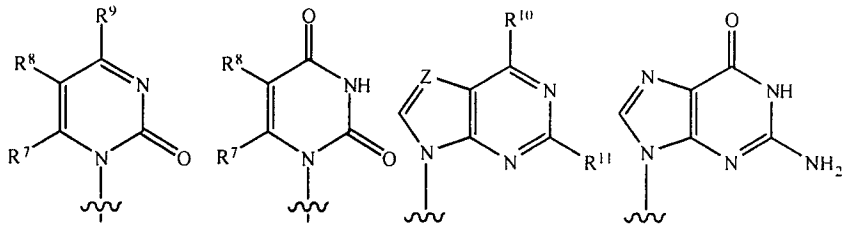
(f) $R^6$ is H, $CH_3$, $CH_2F$, $CHF_2$, $CF_3$, F, or CN;

(g) X is H, OH, F, OMe, halogen, $NH_2$, or $N_3$;

(h) Y is OH, H, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, vinyl, $N_3$, CN, Cl, Br, F, I, $NO_2$, OC(O)O($C_{1-4}$ alkyl), OC(O)O($C_{1-4}$ alkyl), OC(O)O($C_{2-4}$ alkynyl), OC(O)O($C_{2-4}$ alkenyl), O$C_{1-10}$ haloalkyl, O(aminoacyl), O($C_{1-10}$ acyl), O($C_{1-4}$ alkyl), O($C_{2-4}$ alkenyl), S($C_{1-4}$ acyl), S($C_{1-4}$ alkyl), S($C_{2-4}$ alkynyl), S($C_{2-4}$ alkenyl), SO($C_{1-4}$ acyl), SO($C_{1-4}$ alkyl), SO($C_{2-4}$ alkynyl), SO($C_{2-4}$ alkenyl), $SO_2$($C_{1-4}$ acyl), $SO_2$($C_{1-4}$ alkyl), $SO_2$($C_{2-4}$ alkynyl), $SO_2$($C_{2-4}$ alkenyl), $OS(O)_2$($C_{1-4}$ acyl), $OS(O)_2$($C_{1-4}$ alkyl), $OS(O)_2$($C_{2-4}$ alkenyl), $NH_2$, NH($C_{1-4}$ alkyl), NH($C_{2-4}$

alkenyl), NH($C_{2-4}$ alkynyl), NH($C_{1-4}$ acyl), N($C_{1-4}$ alkyl)$_2$, N($C_{1-18}$ acyl)$_2$, wherein alkyl, alkynyl, alkenyl and vinyl are optionally substituted by $N_3$, CN, one to three halogen (Cl, Br, F, I), $NO_2$, C(O)O($C_{1-4}$ alkyl), C(O)O($C_{1-4}$ alkyl), C(O)O($C_{2-4}$ alkynyl), C(O)O($C_{2-4}$ alkenyl), O($C_{1-4}$ acyl), O($C_{1-4}$ alkyl), O($C_{2-4}$ alkenyl), S($C_{1-4}$ acyl), S($C_{1-4}$ alkyl), S($C_{2-4}$ alkynyl), S($C_{2-4}$ alkenyl), SO($C_{1-4}$ acyl), SO($C_{1-4}$ alkyl), SO($C_{2-4}$ alkynyl), SO($C_{2-4}$ alkenyl), $SO_2$($C_{1-4}$ acyl), $SO_2$($C_{1-4}$ alkyl), $SO_2$($C_{2-4}$ alkynyl), $SO_2$($C_{2-4}$ alkenyl), OS(O)$_2$($C_{1-4}$ acyl), OS(O)$_2$($C_{1-4}$ alkyl), OS(O)$_2$($C_{2-4}$ alkenyl), $NH_2$, NH($C_{1-4}$ alkyl), NH($C_{2-4}$ alkenyl), NH($C_{2-4}$ alkynyl), NH($C_{1-4}$ acyl), N($C_{1-4}$ alkyl)$_2$, N($C_{1-4}$ acyl)$_2$;

the base is a naturally occurring or modified purine or pyrimidine base represented by the following structures:



a b c d

wherein

Z is N or $CR^{12}$;

$R^7$, $R^8$,$R^9$, $R^{10}$, and $R^{11}$are independently H, F, Cl, Br, I, OH, OR', SH, SR', $NH_2$, NHR', NR'$_2$, lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$, lower alkynyl of $C_2$-$C_6$ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', CONR'$_2$, CH=CH$CO_2H$, or CH=CH$CO_2R'$,

wherein R' is an optionally substituted alkyl , which includes, but is not limited to, an optionally substituted $C_{1-20}$ alkyl, an optionally substituted $C_{1-10}$ alkyl, an optionally substituted lower alkyl; an optionally substituted cycloalkyl;

an optionally substituted alkynyl of $C_2$-$C_6$, an optionally substituted lower alkenyl of $C_2$-$C_6$, or optionally substituted acyl, which includes but is not limited to C(O) alkyl, C(O)($C_{1-20}$ alkyl), C(O)($C_{1-10}$ alkyl), or C(O)(lower alkyl) or alternatively, in the instance of $NR'_2$, each R' comprise at least one C atom that are joined to form a heterocycle comprising at least two carbon atoms; and

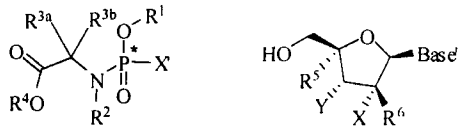
$R^{12}$ is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', $NH_2$, NHR', $NR'_2$, $NO_2$ lower alkyl of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkyl of $C_1$-$C_6$, lower alkenyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkenyl of $C_2$-$C_6$ , lower alkynyl of $C_2$-$C_6$, halogenated (F, Cl, Br, I) lower alkynyl of $C_2$-$C_6$, lower alkoxy of $C_1$-$C_6$, halogenated (F, Cl, Br, I) lower alkoxy of $C_1$-$C_6$, $CO_2H$, $CO_2R'$, $CONH_2$, CONHR', $CONR'_2$, $CH{=}CHCO_2H$, or $CH{=}CHCO_2R'$; with the proviso that when base is represented by the structure c with $R^{11}$ being hydrogen, $R^{12}$ is not a: (i) $-C{\equiv}C-H$, (ii) $-C{=}CH_2$, or (iii) $-NO_2$

and

wherein X' is a leaving group, such as, Cl.

10. A product its stereoisomer, salt, hydrate, solvate or crystalline form thereof, prepared a process comprising:

reacting a substituted phosphochloridate compound **4** with a nucleoside analog **5**



**4** **5** ;

wherein the product comprises a compound, its stereoisomer, salt, hydrate, solvate, or crystalline form thereof, selected from among

**5** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-alanyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester);

**6** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-

yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**7** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**8** 2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-alanyl phosphate (((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester);

**9** $N^4$-(*N,N*-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-*C*-methylcytidine;

**10** 2'-Deoxy-2'-fluoro-2'-C-methylcytidine 5'-(phenyl methoxy-alanyl phosphate (((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenyoxy-phosphorylamino}-propionic acid methyl ester);

**11** 2'-Deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(4-bromophenyl methoxy-valyl phosphate (2'-Deoxy-2'-fluoro-2'-*C*-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate ((S)-2-{(4-bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-3-methyl-butyric acid methyl ester);

**12** 2'-deoxy-2'-fluoro-2'-*C*-methylcytidine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2-oxo-3-amino-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butyric acid methyl ester;

**13** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid ethyl ester;

**14** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid benzyl ester;

**15** {[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-acetic acid methyl ester;

**16** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**17** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino]-propionic acid methyl ester;

**18** (S)-1-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphoryl}-pyrrolidine-2-carboxylic acid methyl ester;

**19** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**20** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**21** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid methyl ester;

**22** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**23** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

**24** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid sec-butyl ester;

**25** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**26** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**27** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid ethyl ester;

**28** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**29** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**30** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;

**31** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid benzyl ester;

**32** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**33** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid isopropyl ester;

**34** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid butyl ester;

**35** (S)-2-{(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**36** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**37** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

**38** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid pentyl ester;

**39** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**40** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**41** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**42** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid butyl ester;

**43** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid benzyl ester;

**44** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid methyl ester;

**45** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 4-fluoro-benzyl ester;

**46** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**47** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 3-methyl-butyl ester;

**48** (S)-2-{(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;

**49** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclohexyl ester;

**50** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;

**51** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;

**52** (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

**53** (S)-2-{(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;

**54** (S)-2-{(4-Bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;

**55** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**56** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-bromo-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

**57** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid isopropyl ester;

**58** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclohexyl ester;

**59** (S)-2-[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-butyric acid cyclohexyl ester;

**60** (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4 R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-butyric acid isopropyl ester;

**61** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2-difluoro-ethyl ester;

**62** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2,2,2-trifluoro-1-trifluoromethyl-ethyl ester;

**63** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 2-fluoro-1-fluoromethyl-ethyl ester;

**64** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo- 3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclopropyl methyl ester;

**65** (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid cyclopentyl ester;

**66** (S)-2-{[(2R,3R,4R,5R)-5-(6-Amino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**67** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-hydroxy-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**68** (S)-2-{(R)-[(2R,3R,4R,5R)-5-(2,6-Diamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**69** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclopentylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**70** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-azetidin-1-yl-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**71** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-diethylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**72** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-propylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**73** (S)-2-{[(2R,3R,4R,5R)-5-(2-Amino-6-cyclobutylamino-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid methyl ester;

**74** (S)-2-({(2R,3R,4R,5R)-5-[2-Amino-6-(4-methyl-piperazin-1-yl)-purin-9-y l]-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy}-phenoxy-p hosphorylamino)-propionic acid methyl ester;

**75** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(propylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**76** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclobutylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**77** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclopentylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**78** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(aziridin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

**79** (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(piperidin-1-yl)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate; and

**80** (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate

wherein Base' is as recited in each of compounds 5-74; and

wherein X' is a leaving group, such as, Cl.

Dated this 20th day of October 2009.

Ganguli

DR. SANCHITA GANGULI
of S. MAJUMDAR & CO.
Applicants' Agent