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;

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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;

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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-phosphorylamino)-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;

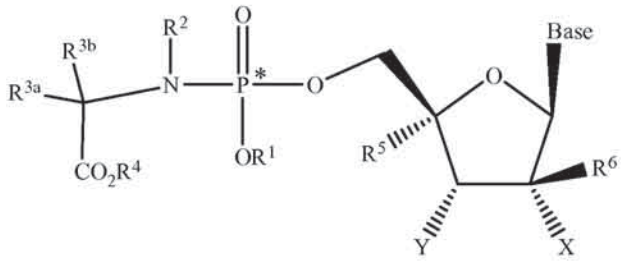
79 (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(piperidin-1-yl)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate; and

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

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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

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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;

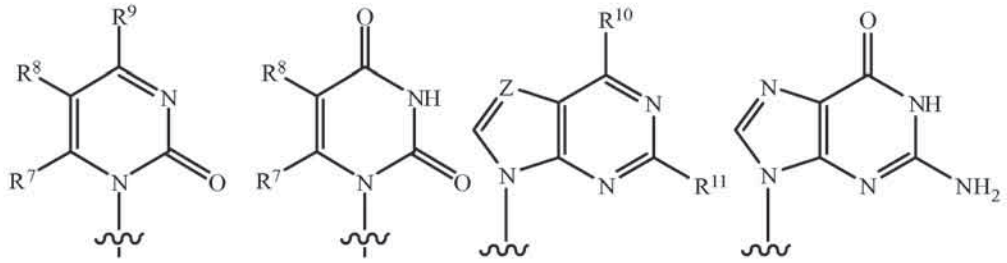
(g) X is H, OH, F, OMe, halogen, NH_2, or N_3;

(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),

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$SO(C_{2-4}$ 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-

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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;

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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;

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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;

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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;

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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;

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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;

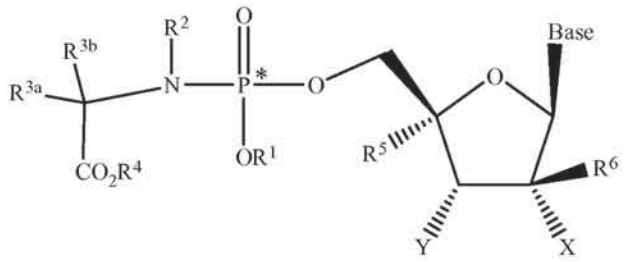
79 (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(piperidin-1-yl)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate; and

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.

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5. A use of the compound represented by formula I in the manufacture of a medicament 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

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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;

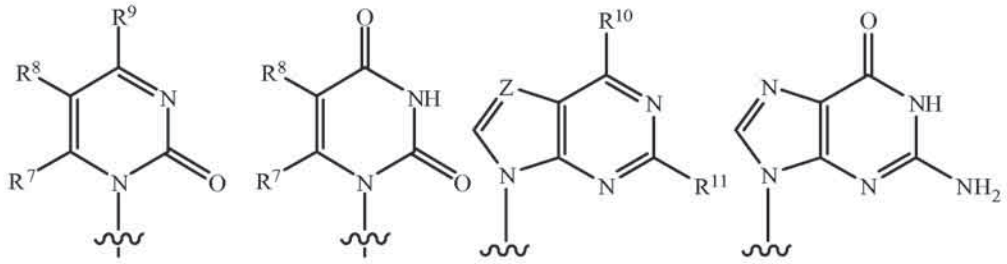
(f) R^6 is H, CH_3, CH_2F, CHF_2, CF_3, F, or CN;

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

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(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};

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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 use of

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-

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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;

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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;

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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;

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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;

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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

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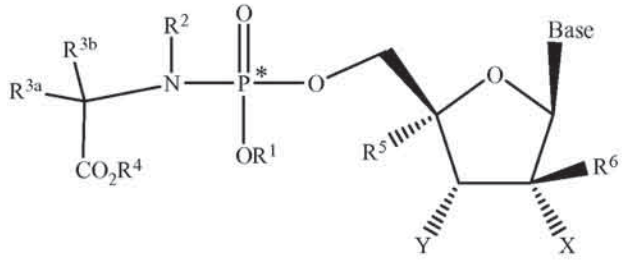
80 (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate

in the manufacture of a medicament 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 method of treatment in a subject in need thereof, which comprises:

administering a therapeutically effective amount of the compound represented by formula I to the subject;

wherein the compound or 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,

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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,

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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;

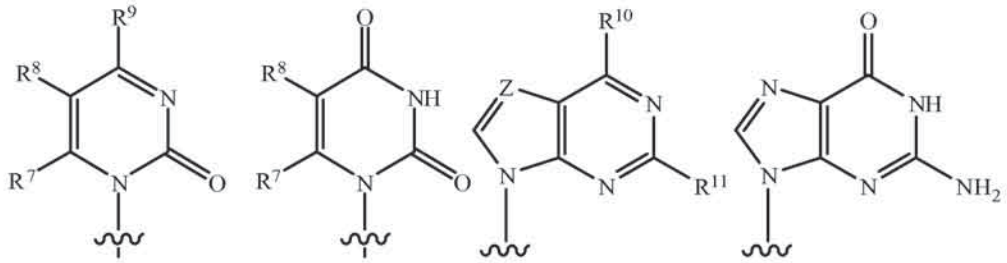
(f) R^6 is H, CH_3, CH_2F, CHF_2, CF_3, F, or CN;

(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:

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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', $CONR'_2$,

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$CH=CHCO_2H$, 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) $-NO_2$.

8. A method of treatment in a subject in need thereof, which comprises:

administering a therapeutically effective amount of 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;

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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;

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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;

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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;

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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;

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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;

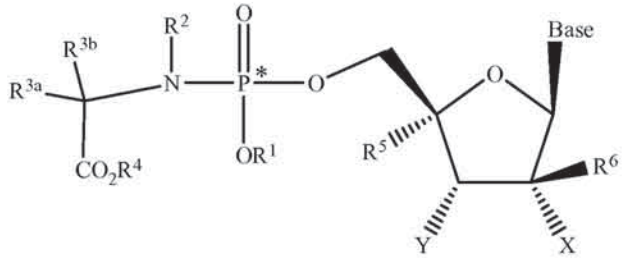
77 (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(cyclopentylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

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.

9. 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,

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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,

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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;

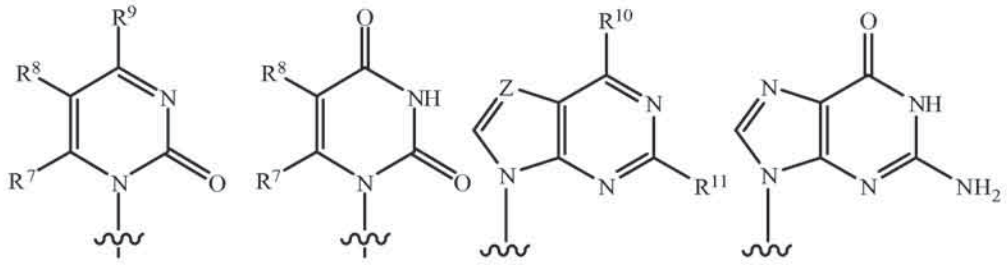
(f) R^6 is H, CH_3, CH_2F, CHF_2, CF_3, F, or CN;

(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:

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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

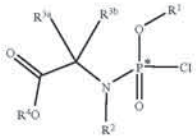
R^{12} is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', NH_2, NHR', NR'_2, NO_2 lower alkyl of C_1-C_6, halogenated (F, Cl, Br, I) lower alkyl of C_1-C_6, lower alkenyl of C_2-C_6, halogenated (F, Cl, Br, I) lower alkenyl of C_2-C_6 , lower alkynyl of C_2-C_6, halogenated (F, Cl, Br, I) lower 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', $CONR'_2$,

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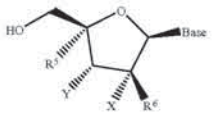
$CH=CHCO_2H$, or $CH=CHCO_2R'$; with the proviso that when base is represented by the structure c with R^{11} being hydrogen, R^{12} is not a: (i) $-C\equiv C-H$, (ii) $-C=CH_2$, or (iii) $-NO_2$;

said process comprising:

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



4



5

10. 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);

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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;

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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;

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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;

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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;

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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-phosphorylamino)-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;

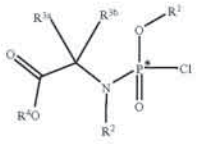
78 (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(aziridin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

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

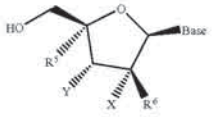
80 (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate

said process comprising:

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



4

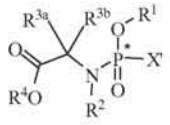


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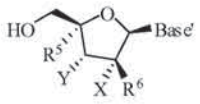
11. A product its stereoisomer, salt, hydrate, solvate or crystalline form thereof, prepared a process comprising:

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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, $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, -

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$CH_2CH_2CH_2NHC(NH)NH_2$, 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;

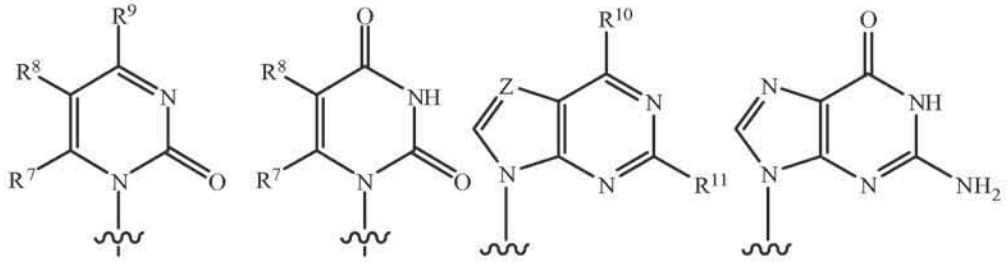
(g) X is H, OH, F, OMe, halogen, NH_2, or N_3;

(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,

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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

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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

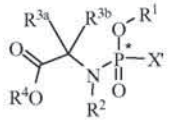
R^{12} is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', NH_2, NHR', NR'_2, NO_2 lower alkyl of C_1-C_6, halogenated (F, Cl, Br, I) lower alkyl of C_1-C_6, lower alkenyl of C_2-C_6, halogenated (F, Cl, Br, I) lower alkenyl of C_2-C_6 , lower alkynyl of C_2-C_6, halogenated (F, Cl, Br, I) lower 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) $–NO_2$

and

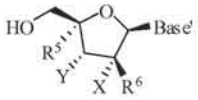
wherein X' is a leaving group, such as, Cl.

12. 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);

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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;

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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;

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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;

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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;

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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;

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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

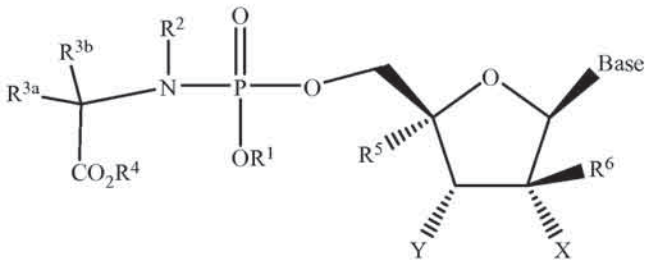
wherein Base' is as recited in each of compounds 5-74; and

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

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ABSTRACT

Disclosed herein are phosphoramidate prodrugs of nucleoside derivatives for the treatment of viral infections in mammals, which is a compound, its stereoisomer, salt (acid or basic addition salt), hydrate, solvate, or crystalline form thereof, represented by the following structure:



I

Also disclosed are methods of treatment, uses, and processes for preparing each of which utilize the compound represented by formula **I**.

Gilead Exhibit 2020
PGR2023-00046 - Page 00748

Electronic Acknowledgement Receipt

EFS ID:	28123921
Application Number:	15411506
International Application Number:	
Confirmation Number:	9714
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	117796
Filer:	Lawrence F. Rozsnyai/Susan Ahearn
Filer Authorized By:	Lawrence F. Rozsnyai
Attorney Docket Number:	PH3080.PC4C2
Receipt Date:	20-JAN-2017
Filing Date:	
Time Stamp:	16:21:50
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal of New Application	PH3080PC4C2_2017-01-20_Appl_Transmittal.PDF	86353 9fd1b930fb2866527f33b410afda7f2f1663e72a	no	1

Warnings:

Information:					
2	Application Data Sheet	PH3080PC4C2_2017-01-20_ADS.PDF	83159 492d7f852806b6c19fb8a28bacbeb5cc74ab01ba	no	7
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
3	Oath or Declaration filed	PH3080PC4CTRK1_2015_03_12_Executed_Decs_as_Filed.PDF	483049 b85fe2d6b661146b267ece594a8b32d30b1dfdda	no	4
Warnings:					
Information:					
4	Specification	PH3080PC4C2_2017-01-20_Part1_Spec_as_Filed.PDF	18886134 a473c0a75bfff11f3eac1b5d085008898b054fc3	no	368
Warnings:					
Information:					
5		PH3080PC4C2_2017-01-20_Part2_Spec_as_Filed.PDF	20343790 4248714c742dcfc83bfad0381eac710cc503736a	yes	368

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Specification	1	311
	Claims	312	367
	Abstract	368	368

Warnings:	
Information:	
Total Files Size (in bytes):	39882485

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Corrected Application Data Sheet

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Correspondence Information

Correspondence Customer Number::	~~124963~~ 117796

Application Information

Application Number::	~~Not Yet Assigned~~ 15/411,506
Application Type::	Regular
Subject Matter::	Utility
CD-ROM or CD-R?::	None
Sequence submission?::	None
Computer Readable Form (CRF)?::	No
Title::	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
Attorney Docket Number::	PH3080.PC4C2
Request for Early Publication?::	No
Request for Non-Publication?::	No
Small Entity?::	No
Petition included?::	No
Portions or all of the application associated with this	No

Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2::

This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013:: No

Representative Information

Representative Customer Number:: ~~124963~~ 117796

Domestic Priority Information

Application::	Continuity Type::	Parent Application::	Parent Filing Date::	Prior Appl Status::
This Application	Continuation of	14/656,546	03/12/15	Pending
14/656,546	Continuation of	14/013,237	08/29/13	Pending
14/013,237	Continuation of	13/609,614	09/11/12	Patented
13/609,614	Continuation of	12/053,015	03/21/08	Patented

Foreign Priority Information

Applicant Information

Applicant Number:: 1

Applicant Type:: Assignee

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Assignee Information Including Non-Applicant Assignee Information

Signature:

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Lawrence F. Rozsnyai/	Date (YYYY-MM-DD)	2017-01-23
Name	Lawrence F. Rozsnyai	Registration Number	58,427

Electronic Acknowledgement Receipt

EFS ID:	28141414
Application Number:	15411506
International Application Number:	
Confirmation Number:	9714
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	117796
Filer:	Lawrence F. Rozsnyai/Susan Ahearn
Filer Authorized By:	Lawrence F. Rozsnyai
Attorney Docket Number:	PH3080.PC4C2
Receipt Date:	23-JAN-2017
Filing Date:	
Time Stamp:	17:56:09
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Application Data Sheet	PH3080PC4C2_2017-01-23_Corrected_ADS.PDF	68693 108e1d83c403183faca7db4b60c89742e481a700	no	6

Warnings:

Information:	
This is not an USPTO supplied ADS fillable form	
Total Files Size (in bytes):	68693

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Docket No.: PH3080.PC4C2
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Jinfa Du et al.

Application No.: 15/411,506 | Confirmation No.: 9714

Filed: January 20, 2017 | Art Unit: 1629

For: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS | Examiner: Not Yet Assigned

PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.115

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

Prior to examination on the merits, please amend the above-identified U.S. patent application as follows:

Amendments to the Specification begin on page 2 of this paper.

Remarks/Arguments begin on page 3 of this paper.

AMENDMENTS TO THE SPECIFICATION

Please insert the following paragraph on page 1 after the title but before the sub-heading "Field of the Invention":

This application is a continuation of U.S. Patent Application No. 14/656,546, filed March 12, 2015, which is a continuation of U.S. Patent Application No. 14/013,237, filed August 29, 2013, now U.S. Patent No. 9,085,573, which is a continuation of U.S. Patent Application No. 13/609,614, filed September 11, 2012, now U.S. Patent No. 8,580,765, which is a continuation of U.S. Application No. 13/099,671, filed May 3, 2011, now U.S. Patent No. 8,334,270, which is a continuation of U.S. Patent Application No. 12/053,015, filed March 21, 2008, now U.S. Patent No. 7,964,580, which claims the benefit under 35 U.S.C. § 1 19(e) to U.S. Provisional Application Nos. 60/909,315, filed March 30, 2007, and 60/982,309, filed October 24, 2007, all of which are hereby incorporated by reference in their entireties.

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REMARKS

Applicant respectfully requests that the foregoing amendments be made prior to examination of the present application. It is believed that no new matter is presented by the foregoing amendments. Favorable consideration of the application as amended is respectfully requested.

Respectfully submitted,

Dated: January 26, 2017

By /Neeta C. Thakur/
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Gilead Exhibit 2020
PGR2023-00046 - Page 00762

Corrected Application Data Sheet

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Gilead Exhibit 2020
PGR2023-00046 - Page 00763

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City of Residence::	San Mateo
State or Province of Residence::	CA
Country of Residence::	US
Street of mailing address::	c/o Gilead Sciences, Inc.
	333 Lakeside Drive

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City of mailing address::	Foster City
State or Province of mailing address::	CA
Country of mailing address::	US
Postal or Zip Code of mailing address::	94404

Correspondence Information

Correspondence Customer Number::	117796

Application Information

Application Number::	15/411,506
Filing Date::	**01/20/17**
Application Type::	Regular
Subject Matter::	Utility
CD-ROM or CD-R?::	None
Sequence submission?::	None
Computer Readable Form (CRF)?::	No
Title::	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
Attorney Docket Number::	PH3080.PC4C2
Request for Early Publication?::	No
Request for Non-Publication?::	No
Small Entity?::	No
Petition included?::	No

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Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2::	No
This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013::	No

Representative Information

Representative Customer Number::	117796

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Domestic Priority Information

Application::	Continuity Type::	Parent Application::	Parent Filing Date::	Prior Appl Status::
~~This application~~ **15/411,506**	Continuation of	14/656,546	03/12/15	Pending
14/656,546	Continuation of	14/013,237 **Now U.S. Patent No. 9,085,573**	08/29/13	~~Pending~~ **Patented**
14/013,237	Continuation of	13/609,614 **Now U.S. Patent No. 8,580,765**	09/11/12	Patented
~~13/609,614~~	~~Continuation of~~	~~12/053,015 Now U.S. Patent No. 7,964,580~~	~~03/21/08~~	~~Patented~~
13/609,614	**Continuation of**	**13/099,671 Now U.S. Patent No. 8,334,270**	**05/03/11**	**Patented**
13/099,671	**Continuation of**	**12/053,015 Now U.S. Patent No. 7,964,580**	**03/21/08**	**Patented**
12/053,015	**An application claiming the benefit under 35 USC 119(e)**	**60/982,309**	**10/24/07**	**Expired**
12/053,015	**An application claiming the benefit under 35 USC 119(e)**	**60/909,315**	**03/30/07**	**Expired**

Foreign Priority Information

Gilead Exhibit 2020
PGR2023-00046 - Page 00767

Applicant Information

Applicant Number::	1
Applicant Type::	Assignee
Organization Name::	Gilead Pharmasset LLC
Street of mailing address::	c/o Gilead Sciences, Inc.
	333 Lakeside Drive
City of mailing address::	Foster City
State or Province of mailing address::	CA
Country of mailing address::	US
Postal or Zip Code of mailing address::	94404
Phone Number::	(650) 574-3000
Fax Number::	(650) 522-5575
E-Mail Address::	IPDocketing@gilead.com

Assignee Information Including Non-Applicant Assignee Information

Gilead Exhibit 2020
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Signature:

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Neeta C. Thakur/	Date (YYYY-MM-DD)	2017-01-26
Name	Neeta C. Thakur	Registration Number	59,123

Gilead Exhibit 2020
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Electronic Acknowledgement Receipt

EFS ID:	28182228
Application Number:	15411506
International Application Number:	
Confirmation Number:	9714
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	117796
Filer:	Neeta C. Thakur/Joannah Laluces
Filer Authorized By:	Neeta C. Thakur
Attorney Docket Number:	PH3080.PC4C2
Receipt Date:	26-JAN-2017
Filing Date:	
Time Stamp:	17:55:33
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Preliminary Amendment	37JD-199059-US9_Preliminary_Amendment.pdf	84927 296e06a8893b1af012fc31df2765e5bc9084b93d	no	3

Warnings:

Information:					
2	Application Data Sheet	37JD-199059-US9_Corrected_Application_Data_Sheet.pdf	70118 50368bca86748de536f1291d1bbd2fc19b611149	no	7
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
			Total Files Size (in bytes):	155045	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 15/411,506	Filing Date 01/20/2017	☐ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	01/26/2017	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 19	Minus	** 20	= 0	X $80 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0	X $420 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LDRC
/EVA GILLIS/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**
If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/411,506	01/20/2017	Jinfa Du	PH3080.PC4C2

CONFIRMATION NO. 9714

117796
Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301

FORMALITIES LETTER

OC000000088828823

Date Mailed: 01/31/2017

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

Items Required To Avoid Abandonment:

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The statutory basic filing fee is missing.
- The application search fee must be submitted.
- The application examination fee must be submitted.

The application is informal since it does not comply with the regulations for the reason(s) indicated below.

The required item(s) identified below must be timely submitted to avoid abandonment:

- A substitute specification in compliance with 37 CFR 1.52, 1.121(b)(3), and 1.125, is required. The substitute specification must be submitted with markings and be accompanied by a clean version (without markings) as set forth in 37 CFR 1.125(c) and a statement that the substitute specification contains no new matter (see 37 CFR 1.125(b)). The specification, claims, and/or abstract page(s) submitted is not acceptable and cannot be scanned or properly stored because:
  - The line spacing on the specification, claims, and/or abstract is not 1½ or double spaced (see 37 CFR 1.52(b)).
- This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c) Applicant must provide an initial paper or compact disc copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application** and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d). If the effective filing date is on or after September 8, 2000, see the final rulemaking notice published in the Federal Register at 65 FR 54604 (September 8, 2000) and 1238 OG 145 (September 19, 2000).
- A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e). If the effective filing date is on or after September 8, 2000, see the final rulemaking notice published in the Federal Register at 65 FR 54604 (September 8, 2000) and 1238 OG 145 (September 19,

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2000). Applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing" and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d). If applicant desires the sequence listing in the instant application to be identical with that of another application on file in the U.S. Patent and Trademark Office, such request in accordance with 37 CFR 1.821(e) may be submitted in lieu of a new CRF.

For questions regarding compliance to these requirements, please contact:

- **For Rules interpretation, call (571) 272-2510**
- **For CRF submission help, call (571) 272-2510**
- **For PatentIn software program support technical assistance, call (866)217-9197.**
- **Send e-mail correspondence for PatentIn software program help to ebc@uspto.gov**
- **Patent software is available at http://www.uspto.gov/patents/resources/tools/checker/patentinrel.jsp .**

Applicant is cautioned that correction of the above items may cause the specification and drawings page count to exceed 100 pages. If the specification and drawings exceed 100 pages, applicant will need to submit the required application size fee.

- Additional claim fees of $ **3780** as an undiscounted entity, including any required multiple dependent claim fee, are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due.
- Surcharge as set forth in 37 CFR 1.16(f) must be submitted.
  The surcharge is due for any one of:
  - late submission of the basic filing fee, search fee, or examination fee,
  - late submission of inventor's oath or declaration,
  - filing an application that does not contain at least one claim on filing, or
  - submission of an application filed by reference to a previously filed application.

SUMMARY OF FEES DUE:

The fee(s) required within **TWO MONTHS** from the date of this Notice to avoid abandonment is/are itemized below. No entity status discount is in effect. If applicant is qualified for small entity status, a written assertion of small entity status must be submitted to establish small entity status. (See 37 CFR 1.27). If applicant is qualified for micro entity status, an acceptable Certification of Micro Entity Status must be submitted to establish micro entity status. (See 37 CFR 1.29 and forms PTO/SB/15A and 15B.)

- $ **280** basic filing fee.
- $ **4000** for **451** electronically equivalent pages in excess of **100** application size fee.
- $ **140** surcharge.
- $ **600** search fee.
- $ **720** examination fee.
- $ **3780** for **9** independent claims over 3.
- $(**0**) previous unapplied payment amount.
- $ **9520** TOTAL FEE BALANCE DUE.

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Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

Replies should be mailed to:

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web, including a copy of this Notice and selecting the document description "Applicant response to Pre-Exam Formalities Notice". https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at 1-866-217-9197 or visit our website at http://www.uspto.gov/ebc.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/fhadera/

Gilead Exhibit 2020
PGR2023-00046 - Page 00775

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
15/411,506	01/20/2017	1629	0.00	PH3080.PC4C2	12	12

CONFIRMATION NO. 9714

117796
Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301

FILING RECEIPT

OC000000088828822

Date Mailed: 01/31/2017

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

Jinfa Du, Redwood City, CA;
Dhanapalan Nagarathnam, Bethany, CT;
Michael Joseph Sofia, Doylestown, PA;
Peiyuan Wang, San Mateo, CA;

Applicant(s)

Gilead Pharmasset LLC, Foster City, CA;

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 14/656,546 03/12/2015
which is a CON of 14/013,237 08/29/2013 PAT 9085573
which is a CON of 13/609,614 09/11/2012 PAT 8580765
which is a CON of 13/099,671 05/03/2011 PAT 8334270
which is a CON of 12/053,015 03/21/2008 PAT 7964580
which claims benefit of 60/982,309 10/24/2007
and claims benefit of 60/909,315 03/30/2007

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

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Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 01/30/2017
The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/411,506**
Projected Publication Date: To Be Determined - pending completion of Missing Parts
Non-Publication Request: No
Early Publication Request: No
Title

NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

Preliminary Class

514

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific

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countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop

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technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 15/411,506

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	280
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	600
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	720
TOTAL CLAIMS (37 CFR 1.16(i))	12 minus 20 =	*			OR	x 80 =	0.00
INDEPENDENT CLAIMS (37 CFR 1.16(h))	12 minus 3 =	* 9				x 420 =	3780
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						4000
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	9380

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: August 29 2017 Signature: /Sylvia Brennan/
(Sylvia Brennan)

Docket No.: PH3080.PC4C2
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Jinfa Du et al.

Application No.: 15/411,506 Confirmation No.:9714

Filed: January 20, 2017 Art Unit: 1629

For: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS Examiner: Not Yet Assigned

DECLARATION PURSUANT TO 37 C.F.R. § 1.821(f)

MS Sequence
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Madam:

I, Lawrence F. Rozsnyai, declare as follows:

1. That the content of the paper and computer readable copies of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.821(c) and (e), respectively, and PCT Rule 5.2, are the same in compliance with 37 C.F.R. § 1.821(f).

2. That all statements made herein of my own knowledge are true and that all statements were made on information and belief and are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: August 29 2017

Respectfully submitted,

By __/Lawrence F. Rozsnyai/__
Lawrence F. Rozsnyai
Registration No.: 58,427
GILEAD PHARMASSET LLC
Correspondence Customer Number: 124963
(650) 577-6841
Attorney For Applicant

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: August 29 2017 Signature: /Sylvia Brennan/
(Sylvia Brennan)

Docket No.: PH3080.PC4C2
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Jinfa Du et al.

Application No.: 15/411,506 Confirmation No.: 9714

Filed: January 20, 2017 Art Unit: 1629

For: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS Examiner: Not Yet Assigned

RESPONSE TO NOTICE TO FILE MISSING PARTS OF APPLICATION

MS Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

In response to the Notice to File Missing Parts of Application, Applicant respectfully submits Amended Claims, a text copy of the Sequence Listing and the Sequence Listing Declaration.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

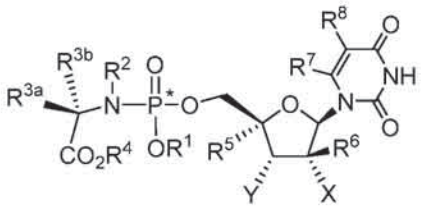
Amendment to Sequence Listing begin on Page 7 of this paper.

Remarks/Arguments begin on page 9 of this paper.

802521

AMENDMENTS TO THE CLAIMS

1. A compound of formula IA:



IA

or a stereoisomer thereof, wherein:

R^1 is naphthyl;

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

R^{3a} and R^{3b} are (i) independently selected from H, 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,

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$CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, 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 H or alkyl and $R^{3''}$ is –OR' or $-N(R^{3'})_2$;

R^4 is H or 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, optionally substituted aryl or optionally substituted heteroaryl;

R^5 is CH_2CN, CH_2NH_2, CH_2NHCH_3 or $CH_2N(CH_3)_2$;

R^6 is H, CH_3, CH_2F, CHF_2, CF_3, F or CN;

X is H, OH, OCH_3, halogen, NH_2, or N_3;

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, 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)$_2$ or $N(C_{1-4}$ acyl)$_2$;

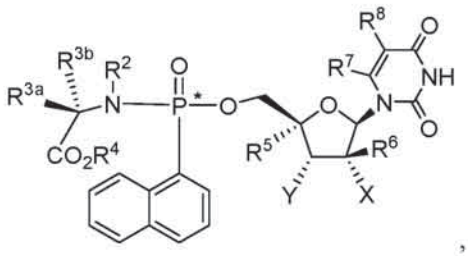
R^7, R^8 and R^9 are independently H, F, Cl, Br, I, OH, OR', SH, SR', NH_2, NHR', NR'$_2$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} haloalkenyl, C_{2-6} alkynyl, C_{2-6} haloalkynyl,

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C_{1-6} alkoxy, C_{1-6} haloalkoxy, CO_2H, CO_2R', $CONH_2$, $CONHR'$, $CONR'_2$, $CH=CHCO_2H$, or $CH=CHCO_2R'$,

wherein R' is an optionally substituted alkyl, an optionally substituted cycloalkyl, an optionally substituted C_{2-6} alkynyl, an optionally substituted C_{2-6} alkenyl, or an optionally substituted acyl, or 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

2. The compound of claim 1 represented by formula 1B:



,

IB

or a stereoisomer thereof.

3. The compound of claim 2, wherein R^2 is H or C_{1-10} alkyl.

4. The compound of claim 2, wherein one of R^{3a} and R^{3b} is H and the other is C_{1-10} alkyl.

5. The compound of claim 2, wherein R^4 is C_{1-10} alkyl.

6. The compound of claim 2, wherein R^6 is methyl.

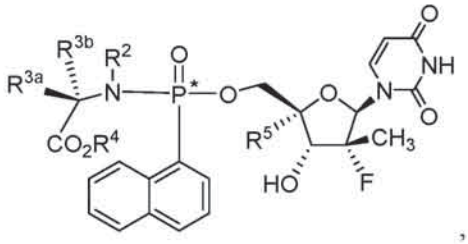
7. The compound of claim 2, wherein each of R^7 and R^8 is H.

8. The compound of claim 2, wherein X is halogen.

9. The compound of claim 2, wherein Y is OH.

10. The compound of claim 2, wherein the compound is represented by formula IC:

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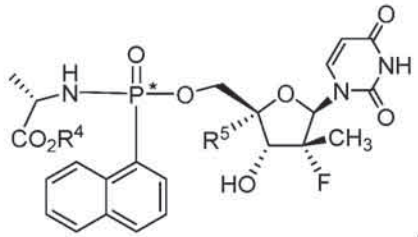


IC

or a stereoisomer thereof.

11. The compound of claim 10, wherein R^2 is H.

12. The compound of claim 10 represented by formula ID:



ID

or a stereoisomer thereof.

13. The compound of claim 12, wherein R^4 is ^{i}Pr, ^{n}Pr, ^{n}Bu, 2-butyl, ^{t}Bu or benzyl.

14. A pharmaceutical composition comprising a compound according to claim 1 and a pharmaceutically acceptable excipient.

15. A method of treating HCV comprising administering a therapeutically effective amount of a compound according to claim 1 to a human in need thereof.

16. The method of claim 15 further comprising administering to the human a therapeutically effective amount of a second antiviral agent.

17. The method of claim 16 wherein the second antiviral agent is an NS5A inhibitor.

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PGR2023-00046 - Page 00787

18. The method of claim 16 wherein the second antiviral agent is an NS3 protease inhibitor.

19. The method of claim 15 further comprising administering to the human subject therapeutically effective amounts of an NS5A inhibitor and an NS3 protease inhibitor.

Gilead Exhibit 2020
PGR2023-00046 - Page 00788

37 C.F.R. § 1.825(a) AMENDMENT TO SEQUENCE LISTING

IN THE SPECIFICATION:

Please amend the specification as shown:

Please insert the following on page 1, after the title:

Sequence Listing

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety.

Please delete the paragraph on page 675, lines 1-17 and replace it with the following paragraph:

EXAMPLE 82

HCV replicon assay. HCV replicon RNA-containing Huh7 cells (clone A cells; Apath, LLC, St. Louis, Mo.) were kept at exponential growth in Dulbecco's modified Eagle's medium (high glucose) containing 10% fetal bovine serum, 4mM L-glutamine and 1mM sodium pyruvate, 1× nonessential amino acids, and G418 (1,000 μg/ml). Antiviral assays were performed in the same medium without G418. Cells were seeded in a 96-well plate at 1,500 cells per well, and test compounds were added immediately after seeding. Incubation time 4 days. At the end of the incubation step, total cellular RNA was isolated (RNeasy 96 kit; Qiagen). Replicon RNA and an internal control (TaqMan rRNA control reagents; Applied Biosystems) were amplified in a single-step multiplex RT-PCR protocol as recommended by the manufacturer. The HCV primers and probe were designed with Primer Express software (Applied Biosystems) and covered highly conserved 5'-untranslated region (UTR) sequences (sense 5'-AGCCATGGCGTTAGTA(T)GAGTGT-3' **(SEQ ID NO: 1)**, and antisense, 5'-

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PGR2023-00046 - Page 00789

TTCCGCAGACCACTATGG-3' **(SEQ ID NO: 2)**; probe, 5'-FAM-CCTCCAGGACCCCCCCTCCC-TAMRA-3' **(SEQ ID NO: 3)**).

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PGR2023-00046 - Page 00790

REMARKS

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicant requests for required fees to be charged our Deposit Account No. 50-6480, under Order No. PH3080.PC4C2 from which the undersigned is authorized to draw. The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-6480. Additional extensions of time are needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-6480.

Dated: August 29, 2017

Respectfully submitted,

Signature: /Lawrence F. Rozsnyai/
Lawrence F. Rozsnyai
Registration No.: 58,427
GILEAD SCIENCES, INC.
Correspondence Customer Number: 124963
(650) 577-6841
Attorney For Applicant

Gilead Exhibit 2020
PGR2023-00046 - Page 00791

Electronic Patent Application Fee Transmittal

Application Number:	15411506
Filing Date:	20-Jan-2017
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Filer:	Lawrence F. Rozsnyai/Sylvia Brennan
Attorney Docket Number:	PH3080.PC4C2

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
UTILITY APPLICATION FILING	1011	1	280	280
UTILITY SEARCH FEE	1111	1	600	600
UTILITY EXAMINATION FEE	1311	1	720	720
Pages:				
Claims:				
Miscellaneous-Filing:				
LATE FILING FEE FOR OATH OR DECLARATION	1051	1	140	140
Petition:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 5 months with $0 paid	1255	1	3000	3000
Miscellaneous:				
		Total in USD ($)		**4740**

Electronic Acknowledgement Receipt	
EFS ID:	30210302
Application Number:	15411506
International Application Number:	
Confirmation Number:	9714
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	117796
Filer:	Lawrence F. Rozsnyai/Sylvia Brennan
Filer Authorized By:	Lawrence F. Rozsnyai
Attorney Docket Number:	PH3080.PC4C2
Receipt Date:	29-AUG-2017
Filing Date:	20-JAN-2017
Time Stamp:	12:28:15
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$4740
RAM confirmation Number	082917INTEFSW00010808506480
Deposit Account	506480
Authorized User	Sylvia Brennan
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: 37 CFR 1.16 (National application filing, search, and examination fees) 37 CFR 1.17 (Patent application and reexamination processing fees)	

37 CFR 1.19 (Document supply fees)

37 CFR 1.20 (Post Issuance fees)

37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Response to Pre-Exam Sequence Notice	PH3080PC4C2_2017_08_29_DecSeqListing_asFiled.PDF	105959 a09dda9e5c2672d4bc61c72c271c43198f1a8b2c	no	2
Warnings:					
Information:					
2	Supplemental Response or Supplemental Amendment	PH3080PC4C2_2017_08_29_RsptoMP_asFiled.PDF	139798 a07435d70548ad45febc2ba8812b5a4d00136393	no	9
Warnings:					
Information:					
3	Sequence Listing (Text File)	PH3080PC4C2_2017_08_28_SequenceListing_asFiled.TXT	1252	no	-
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	39099 2f6962fb0367caed950799e29389e990284edf25	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	286108		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: August 29 2017 Signature: /Sylvia Brennan/
(Sylvia Brennan)

Docket No.: PH3080.PC4C2
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Jinfa Du et al.

Application No.: 15/411,506 Confirmation No.: 9714

Filed: January 20, 2017 Art Unit: 1629

For: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS Examiner: Not Yet Assigned

RESPONSE TO NOTICE TO FILE MISSING PARTS OF APPLICATION

MS Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

In response to the Notice to File Missing Parts of Application, Applicant respectfully submits Amended Claims, a text copy of the Sequence Listing and the Sequence Listing Declaration.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Amendment to Sequence Listing begin on Page 7 of this paper.

Remarks/Arguments begin on page 9 of this paper.

802521

DocCode – SEQ.TXT

SCORE Placeholder Sheet for IFW Content

Application Number: 15411506 Document Date: 08/29/2017

The presence of this form in the IFW record indicates that the following document type was received in electronic format on the date identified above. This content is stored in the SCORE database.

Since this was an electronic submission, there is no physical artifact folder, no artifact folder is recorded in PALM, and no paper documents or physical media exist. The TIFF images in the IFW record were created from the original documents that are stored in SCORE.

- Sequence Listing

At the time of document entry (noted above):

- USPTO employees may access SCORE content via eDAN using the Supplemental Content tab, or via the SCORE web page.
- External customers may access SCORE content via PAIR using the Supplemental Content tab.

Form Revision Date: August 26, 2013

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 15/411,506	Filing Date 01/20/2017	☐ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

AMENDMENT	08/29/2017	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 19	Minus	** 20	= 0	X $80 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0	X $420 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LDRC
/EVA GILLIS/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**
If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

```
============================================================
Sequence Listing could not be accepted due to errors.
See attached Validation Report.
If you need help call the Patent Electronic Business Center at (866)
217-9197 (toll free).
Reviewer: Anjum, Durreshwar
Timestamp: [year=2017; month=9; day=8; hr=9; min=34; sec=9; ms=711; ]
============================================================


************************************************************
Reviewer Comments:
NOTE:  This error report refers to the sequence listing CRF received by
the USPTO on:8/29/2017

1.


E202            Invalid input format; Value must be an integerin <160>
E104            Command to process tag does not exist: Tag: <161> in
Header
E248            Order Sequence Error <160> -> <161>; Expected Mandatory
Tag: <210> in Header
E104            Command to process tag does not exist: Tag: <171> in
Header
E248            Order Sequence Error <170> -> <171>; Expected Mandatory
Tag: <210> in Header
E104            Command to process tag does not exist: Tag: <180> in
Header
E104            Command to process tag does not exist: Tag: <181> in
Header
E104            Command to process tag does not exist: Tag: <190> in
Header
E104            Command to process tag does not exist: Tag: <191> in
Header
E104            Command to process tag does not exist: Tag: <200> in
Header
E202            Invalid input format; Value must be an integerin <210>
in SEQID (0)
E248            Order Sequence Error <210> -> <220>; Expected Mandatory
Tag: <211> in Header
```

```
E311            Invalid field content in <220> in SEQ ID (0)
E104            Command to process tag does not exist: Tag: <230> in
Header
E248            Order Sequence Error <220> -> <230>; Expected Mandatory
Tag: <400> in Header
E104            Command to process tag does not exist: Tag: <240> in
Header
E104            Command to process tag does not exist: Tag: <241> in
Header
E104            Command to process tag does not exist: Tag: <242> in
Header
E104            Command to process tag does not exist: Tag: <243> in
Header
E104            Command to process tag does not exist: Tag: <250> in
Header
E104            Command to process tag does not exist: Tag: <253> in
Header
E212            Invalid Sequence ID Number in <400> SEQID: (0)
E104            Command to process tag does not exist: Tag: <240> in
Header
E104            Command to process tag does not exist: Tag: <241> in
Header
E104            Command to process tag does not exist: Tag: <242> in
Header
E104            Command to process tag does not exist: Tag: <243> in
Header
E104            Command to process tag does not exist: Tag: <250> in
Header
E104            Command to process tag does not exist: Tag: <253> in
Header
E212            Invalid Sequence ID Number in <400> SEQID: (0)
E212            Invalid Sequence ID Number in <400> SEQID: (0)
E252            Calc# of Seq. differs from actual; 0 seqIds defined;
count=1
E250            Structural Validation Error; Sequence listing may not be
indexable


The multiple errors shown above appears in the sequence listing has
wrong designated identifiers
Please follow the instructions below:
```

Numeric Identifier "<150>-<151>" can be used multiple times to insert Prior Application Numbers, please change "<160-<161>, <170>-<171>,<180>-<181>,<190>-<191>,<200>-<210>" to <150>-<151>".
Numeric Identifier "<160>" represents total number of sequences in the sequence listing.
Numeric Identifier "<170>" represents software type used to generate the sequences.

For SEQ ID# 1-3 the numeric identifiers inserted are invalid. Please follow the instructions below using example for SEQ ID# 1. Please make all necessary corrections.

<210> 1
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 1
agccatggcg ttagtatgag tgt
23

Note:

For any sequence listing-related questions or concerns the Applicant is invited to contact the USPTO Sequence Help Desk at 571-272-2510.

The errors listed above are exemplary and may not be a complete list of all errors in the sequence listing file.

To correct the sequence listing errors noted in this report - The recommended method for correction of errors is to access the sequence listing working file using the software program in which the listing was originally prepared, e.g., the project file in PatentIn, make any necessary corrections within that program, then generate a new sequence listing file. Use of a word processing program to correct errors directly in the original sequence listing file is strongly discouraged,

since such programs often introduce unintended changes to the sequence listing, rendering the listing unacceptable. When the working file or original program is not available for correction, then use of a common or plain text-only editor, such as Notepad, to edit the original sequence listing file may suffice.

A sequence listing text file submitted via EFS-Web that complies with the requirements of 37 CFR 1.824(a) (2)-(6) and (b) (i.e., is a compliant sequence listing ASCII text file), serves as both the paper copy required by 37 CFR 1.821(c) and the CRF required by 37 CFR 1.821(e).

****

Validated By CRFValidator v 1.0.5

Application No: 15411506 Version No: 1.0

Input Set:

Output Set:

Started: 2017-08-29 12:33:46.547
Finished: 2017-08-29 12:33:49.578
Elapsed: 0 hr(s) 0 min(s) 3 sec(s) 31 ms
Total Warnings: 0
Total Errors: 42
No. of SeqIDs Defined: 0
Actual SeqID Count: 1

Error code	Error Description
E 202	Invalid input format; Value must be an integerin <160>
E 104	Command to process tag does not exist: Tag: <161> in Header
E 248	Order Sequence Error <160> -> <161>; Expected Mandatory Tag: <210> in Header
E 104	Command to process tag does not exist: Tag: <171> in Header
E 248	Order Sequence Error <170> -> <171>; Expected Mandatory Tag: <210> in Header
E 104	Command to process tag does not exist: Tag: <180> in Header
E 104	Command to process tag does not exist: Tag: <181> in Header
E 104	Command to process tag does not exist: Tag: <190> in Header
E 104	Command to process tag does not exist: Tag: <191> in Header
E 104	Command to process tag does not exist: Tag: <200> in Header
E 202	Invalid input format; Value must be an integerin <210> in SEQID
E 248	Order Sequence Error <210> -> <220>; Expected Mandatory Tag: <211> in Header
E 311	Invalid field content in <220> in SEQ ID (0)
E 104	Command to process tag does not exist: Tag: <230> in Header
E 248	Order Sequence Error <220> -> <230>; Expected Mandatory Tag: <400> in Header
E 104	Command to process tag does not exist: Tag: <240> in Header
E 104	Command to process tag does not exist: Tag: <241> in Header
E 104	Command to process tag does not exist: Tag: <242> in Header

Input Set:

Output Set:

Started: 2017-08-29 12:33:46.547
Finished: 2017-08-29 12:33:49.578
Elapsed: 0 hr(s) 0 min(s) 3 sec(s) 31 ms
Total Warnings: 0
Total Errors: 42
No. of SeqIDs Defined: 0
Actual SeqID Count: 1

Error code	Error Description
E 104	Command to process tag does not exist: Tag: <243> in Header
E 104	Command to process tag does not exist: Tag: <250> in Header
E 104	Command to process tag does not exist: Tag: <253> in Header
E 212	Invalid Sequence ID Number in <400> SEQID: (0)
E 104	Command to process tag does not exist: Tag: <240> in Header
E 104	Command to process tag does not exist: Tag: <241> in Header
E 104	Command to process tag does not exist: Tag: <242> in Header
E 104	Command to process tag does not exist: Tag: <243> in Header
E 104	Command to process tag does not exist: Tag: <250> in Header
E 104	Command to process tag does not exist: Tag: <253> in Header This error has occured more than 20 times, will not be displayed
E 212	Invalid Sequence ID Number in <400> SEQID: (0)
E 212	Invalid Sequence ID Number in <400> SEQID: (0)
E 252	Calc# of Seq. differs from actual; 0 seqIds defined; count=1
E 250	Structural Validation Error; Sequence listing may not be indexable

SEQUENCE LISTING

<110> DU, JINFA
NAGARATHNAM, DHANAPALAN
SOFIA, MICHAEL JOSEPH
WANG, PEIYUAN

<120> NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

<130> PH3080.PC4C2

<140> 14/656,546
<141> 2015-03-12

<150> 14/013,237
<151> 2013-08-29

<160> 13/609,614
<161> 2012-09-11

<170> 13/099,671
<171> 2011-05-03

<180> 12/053,015
<181> 2008-03-21

<190> 60/982,309
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<200> 60/909,315
<210> 2007-03-30

<220> 3

<230> PatentIn version 3.5

<240> 1
<241> 23
<242> DNA
<243> Artificial Sequence

<250>
<253> Description of Artificial Sequence: Synthetic
primer

<400> 1
agccatggcg ttagtatgag tgt 23

<240> 2
<241> 18
<242> DNA
<243> Artificial Sequence

<250>
<253> Description of Artificial Sequence: Synthetic

primer

<400> 2
ttccgcagac cactatgg 18

<240> 3
<241> 20
<242> DNA
<243> Artificial Sequence

<250>
<253> Description of Artificial Sequence: Synthetic probe

<260>
<263> 5'-FAM

<260>
<263> 3'-TAMRA

<400> 3
cctccaggac ccccctccc 20

Electronic Acknowledgement Receipt

EFS ID:	30348596
Application Number:	15411506
International Application Number:	
Confirmation Number:	9714
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	117796
Filer:	Lawrence F. Rozsnyai/Sylvia Brennan
Filer Authorized By:	Lawrence F. Rozsnyai
Attorney Docket Number:	PH3080.PC4C2
Receipt Date:	13-SEP-2017
Filing Date:	20-JAN-2017
Time Stamp:	12:21:32
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Sequence Listing (Text File)	PH3080PC4C2_2017_09_13_CorrectedSeq_Listing_as_filed.TXT	1216	no	-

Warnings:

Information:	
Total Files Size (in bytes):	1216

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

DocCode – SEQ.TXT

SCORE Placeholder Sheet for IFW Content

Application Number: 15411506 Document Date: 09/13/2017

The presence of this form in the IFW record indicates that the following document type was received in electronic format on the date identified above. This content is stored in the SCORE database.

Since this was an electronic submission, there is no physical artifact folder, no artifact folder is recorded in PALM, and no paper documents or physical media exist. The TIFF images in the IFW record were created from the original documents that are stored in SCORE.

- Sequence Listing

At the time of document entry (noted above):

- USPTO employees may access SCORE content via eDAN using the Supplemental Content tab, or via the SCORE web page.
- External customers may access SCORE content via PAIR using the Supplemental Content tab.

Form Revision Date: August 26, 2013

```
============================================================
Sequence Listing was accepted.
If you need help call the Patent Electronic Business Center at (866)
217-9197 (toll free).
Reviewer: Anjum, Durreshwar
Timestamp: [year=2017; month=9; day=15; hr=13; min=25; sec=24; ms=501; ]
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Validated By CRFValidator v 1.0.5

Application No: 15411506 Version No: 2.0

Input Set:

Output Set:

Started: 2017-09-13 13:00:10.863
Finished: 2017-09-13 13:00:11.025
Elapsed: 0 hr(s) 0 min(s) 0 sec(s) 162 ms
Total Warnings: 3
Total Errors: 0
No. of SeqIDs Defined: 3
Actual SeqID Count: 3

Error code	Error Description
W 213	Artificial or Unknown found in <213> in SEQ ID (1)
W 213	Artificial or Unknown found in <213> in SEQ ID (2)
W 213	Artificial or Unknown found in <213> in SEQ ID (3)

SEQUENCE LISTING

<110> DU, JINFA
NAGARATHNAM, DHANAPALAN
SOFIA, MICHAEL JOSEPH
WANG, PEIYUAN

<120> NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

<130> PH3080.PC4C-TRK1

<140> US 15/411,506
<141> 2017-01-20

<150> 14/013,237
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<151> 2012-09-11

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<151> 2011-05-03

<150> 12/053,015
<151> 2008-03-21

<150> 60/982,309
<151> 2007-10-24

<150> 60/909,315
<151> 2007-03-30

<160> 3

<170> PatentIn version 3.5

<210> 1
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 1
agccatggcg ttagtatgag tgt 23

<210> 2
<211> 18
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<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 2
ttccgcagac cactatgg 18

<210> 3
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
probe

<220>
<223> 5'-FAM

<220>
<223> 3'-TAMRA

<400> 3
cctccaggac ccccctccc 20

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
15/411,506	01/20/2017	1629	5740	PH3080.PC4C2	19	1

CONFIRMATION NO. 9714

UPDATED FILING RECEIPT

117796
Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301

OC000000094294804

Date Mailed: 09/25/2017

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

Jinfa Du, Redwood City, CA;
Dhanapalan Nagarathnam, Bethany, CT;
Michael Joseph Sofia, Doylestown, PA;
Peiyuan Wang, San Mateo, CA;

Applicant(s)

Gilead Pharmasset LLC, Foster City, CA;

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 14/656,546 03/12/2015 PAT 9585906
which is a CON of 14/013,237 08/29/2013 PAT 9085573
which is a CON of 13/609,614 09/11/2012 PAT 8580765
which is a CON of 13/099,671 05/03/2011 PAT 8334270
which is a CON of 12/053,015 03/21/2008 PAT 7964580
which claims benefit of 60/982,309 10/24/2007
and claims benefit of 60/909,315 03/30/2007

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Gilead Exhibit 2020
PGR2023-00046 - Page 00815

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 01/30/2017
The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/411,506**
Projected Publication Date: 01/04/2018
Non-Publication Request: No
Early Publication Request: No
Title

NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

Preliminary Class

514

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific

Gilead Exhibit 2020
PGR2023-00046 - Page 00816

countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop

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technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

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PGR2023-00046 - Page 00818

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 15/411,506

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	280
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	600
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	720
TOTAL CLAIMS (37 CFR 1.16(i))	19 minus 20 =	*			OR	x 80 =	0.00
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*				x 420 =	0.00
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						4000
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	5600

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/411,506	01/20/2017	Jinfa Du	PH3080.PC4C2

CONFIRMATION NO. 9714

117796
Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301

PUBLICATION NOTICE



Title:NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

Publication No.US-2018-0000855-A1
Publication Date:01/04/2018

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently https://portal.uspto.gov/pair/PublicPair. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

Gilead Exhibit 2020
PGR2023-00046 - Page 00820

PTO/AIA/80 (07-12)
Approved for use through 11/30/2014. OMB 0651-0035
U.S. Patent and Trademark Office: U.S DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(c).

I hereby appoint:

☒ Practitioners associated with Customer Number: 117796

OR

☐ Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number	Name	Registration Number

As attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignments documents attached to this form in accordance with 37 CFR 3.73(c).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(c) to:

☒ The address associated with Customer Number: 117796

OR

☐

Firm or Individual Name			
Address			
City		State	Zip
Country			
Telephone		Email	

Assignee Name and Address: Gilead Pharmasset LLC
c/o Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

A copy of this form, together with a statement under 37 CFR 3.73(c) (Form PTO/AIA/96 or equivalent) is required to be Filed in each application in which this form is used. The statement under 37 CFR 3.73(c) may be completed by one of The practitioners appointed in this form, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record
The individual whose signature and title is supplied below is authorized to act on behalf of the assignee

Signature		Date	March 4, 2014
Name	J. Elin Hartrum	Telephone	650-522-1871
Title	Associate General Counsel, Intellectual Property		

This collection of information is required by 37 CFR 1.31, 1.32 and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: Gilead Pharmasset LLC

Application No./Patent No.: 15/411506 Filed/Issue Date: 01/20/2017

Titled: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

Gilead Pharmasset LLC (Name of Assignee), a corporation (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. [X] The assignee of the entire right, title, and interest.

2. [ ] An assignee of less than the entire right, title, and interest (check applicable box):

   [ ] The extent (by percentage) of its ownership interest is _____ %). Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.

   [ ] There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. [ ] The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. [ ] The recipient, via a court proceeding or the like (*e.g.*, bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

A. [ ] An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel _____, Frame _____, or for which a copy thereof is attached.

B. [X] A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: Michael Joseph Sofia et al. To: Pharmasset, Inc.
   The document was recorded in the United States Patent and Trademark Office at
   Reel 044268, Frame 0993, or for which a copy thereof is attached.

2. From: Pharmasset, Inc. To: Gilead Pharmasset LLC
   The document was recorded in the United States Patent and Trademark Office at
   Reel 044591, Frame 0279, or for which a copy thereof is attached.

PTO/AIA/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

STATEMENT UNDER 37 CFR 3.73(c)

3. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____ , Frame _____ , or for which a copy thereof is attached.

4. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____ , Frame _____ , or for which a copy thereof is attached.

5. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____ , Frame _____ , or for which a copy thereof is attached.

6. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____ , Frame _____ , or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☒ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/Lorna L. Tanner/	April 2, 2018
Signature	Date
Lorna L. Tanner	50,782
Printed or Typed Name	Title or Registration Number

Corrected Application Data Sheet

Inventor Information

Inventor Number::	1
Given Name::	Jinfa
Family Name::	Du
City of Residence::	Redwood City
State or Province of Residence::	CA
Country of Residence::	US
Street of mailing address::	813 Bay Harbor Drive
City of mailing address::	Redwood City
State or Province of mailing address::	CA
Country of mailing address::	US
Postal or Zip Code of mailing address::	94065

Inventor Number::	2
Given Name::	Dhanapalan
Family Name::	Nagarathnam
City of Residence::	Bethany
State or Province of Residence::	CT
Country of Residence::	US
Street of mailing address::	52 Virginia Rail Drive
City of mailing address::	Bethany
State or Province of mailing address::	CT

Gilead Exhibit 2020
PGR2023-00046 - Page 00824

Country of mailing address::	US
Postal or Zip Code of mailing address::	06524

Inventor Number::	3
Given Name::	Michael
Middle Name::	Joseph
Family Name::	Sofia
City of Residence::	Doylestown
State or Province of Residence::	PA
Country of Residence::	US
Street of mailing address::	3066 Antler Drive
City of mailing address::	Doylestown
State or Province of mailing address::	PA
Country of mailing address::	US
Postal or Zip Code of mailing address::	18902

Inventor Number::	4
Given Name::	Peiyuan
Family Name::	Wang
City of Residence::	San Mateo
State or Province of Residence::	CA
Country of Residence::	US
Street of mailing address::	c/o Gilead Sciences, Inc.

Gilead Exhibit 2020
PGR2023-00046 - Page 00825

	333 Lakeside Drive
City of mailing address::	Foster City
State or Province of mailing address::	CA
Country of mailing address::	US
Postal or Zip Code of mailing address::	94404

Correspondence Information

Correspondence Customer Number::	117796

Application Information

Application Number::	15/411,506
Filing Date::	01/20/17
Application Type::	Regular
Subject Matter::	Utility
CD-ROM or CD-R?::	None
Sequence submission?::	None
Computer Readable Form (CRF)?::	No
Title::	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
Attorney Docket Number::	~~PH3080.PC4C2~~ 37JD-199059-US9
Request for Early Publication?::	No
Request for Non-Publication?::	No
Small Entity?::	No
Petition included?::	No

Gilead Exhibit 2020
PGR2023-00046 - Page 00826

Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2::	No
This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013::	No

Representative Information

Representative Customer Number::	117796

Gilead Exhibit 2020
PGR2023-00046 - Page 00827

Domestic Priority Information

Application::	Continuity Type::	Parent Application::	Parent Filing Date::	Prior Appl Status::
15/411,506	Continuation of	14/656,546	03/12/15	Pending
14/656,546	Continuation of	14/013,237 Now U.S. Patent No. 9,085,573	08/29/13	Patented
14/013,237	Continuation of	13/609,614 Now U.S. Patent No. 8,580,765	09/11/12	Patented
13/609,614	Continuation of	13/099,671 Now U.S. Patent No. 8,334,270	05/03/11	Patented
13/099,671	Continuation of	12/053,015 Now U.S. Patent No. 7,964,580	03/21/08	Patented
12/053,015	An application claiming the benefit under 35 USC 119(e)	60/982,309	10/24/07	Expired
12/053,015	An application claiming the benefit under 35 USC 119(e)	60/909,315	03/30/07	Expired

Foreign Priority Information

Applicant Information

Applicant Number::	1
Applicant Type::	Assignee
Organization Name::	Gilead Pharmasset LLC
Street of mailing address::	c/o Gilead Sciences, Inc.

Gilead Exhibit 2020
PGR2023-00046 - Page 00828

	333 Lakeside Drive
City of mailing address::	Foster City
State or Province of mailing address::	CA
Country of mailing address::	US
Postal or Zip Code of mailing address::	94404
~~Phone Number::~~	~~(650) 574-3000~~
~~Fax Number::~~	~~(650) 522-5575~~
~~E-Mail Address::~~	~~IPDocketing@gilead.com~~

Assignee Information Including Non-Applicant Assignee Information

Signature:

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Lorna L. Tanner/	Date (YYYY-MM-DD)	2018-04-02
Name	Lorna L. Tanner	Registration Number	50,782

Gilead Exhibit 2020
PGR2023-00046 - Page 00830

Electronic Acknowledgement Receipt

EFS ID:	32226057
Application Number:	15411506
International Application Number:	
Confirmation Number:	9714
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	117796
Filer:	Lorna Lea Tanner/stacy okoro
Filer Authorized By:	Lorna Lea Tanner
Attorney Docket Number:	PH3080.PC4C2
Receipt Date:	02-APR-2018
Filing Date:	20-JAN-2017
Time Stamp:	19:24:47
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Power of Attorney	192486-US6_POA.pdf	300194 08c2d6b2dafc8259df57f2413ce20650d239178f	no	10

Warnings:

Information:	
Total Files Size (in bytes):	300194

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/411,506	01/20/2017	Jinfa Du	37JD-199059-US9

CONFIRMATION NO. 9714

117796
Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301

POA ACCEPTANCE LETTER

OC000000098548991

Date Mailed: 04/05/2018

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/02/2018.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/yteferra/

Gilead Exhibit 2020
PGR2023-00046 - Page 00833

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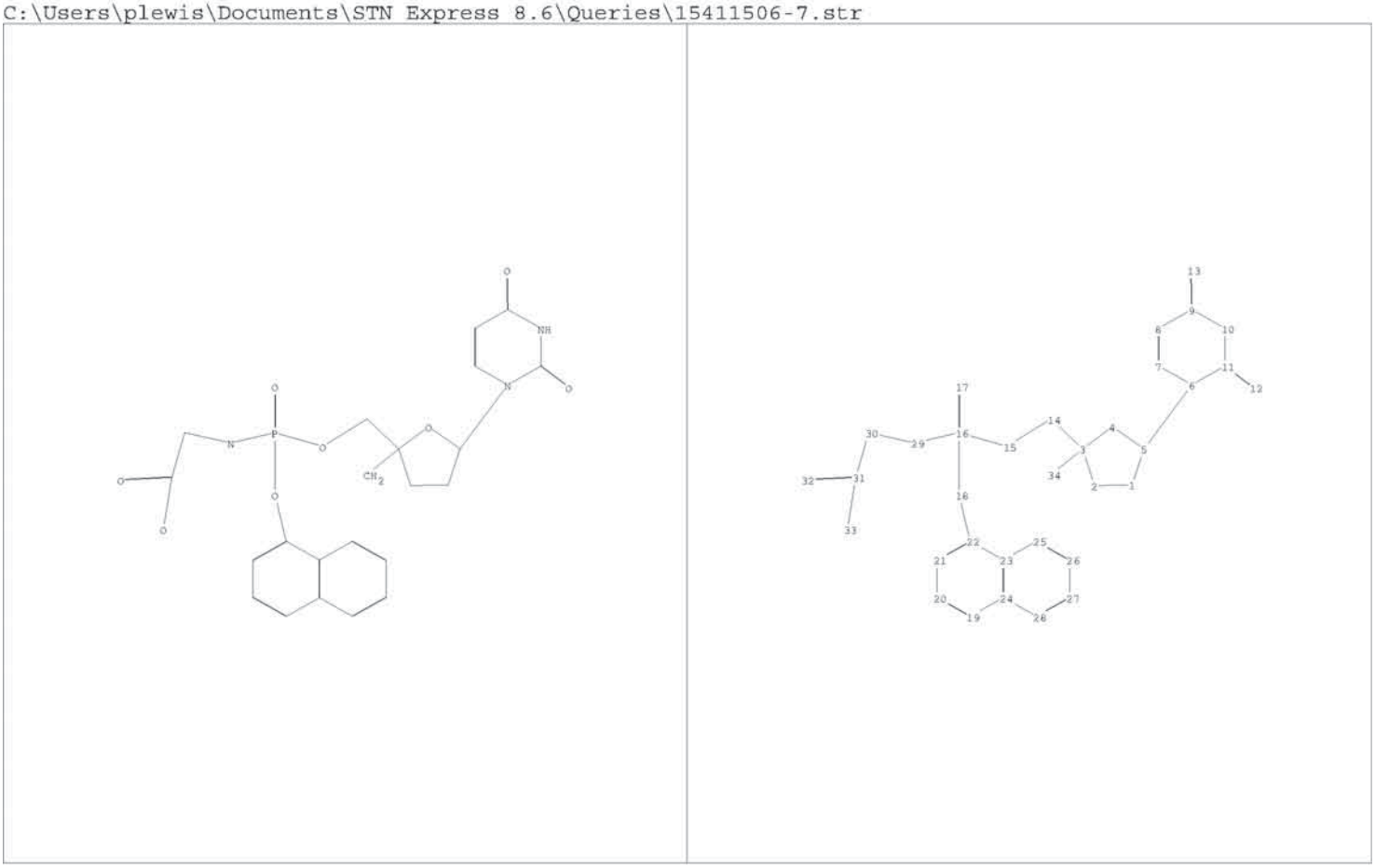
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L3           4 S L1 SSS FULL

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L4           1 S L3

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L6           0 S L5 SSS SAM
L7           8 S L5 SSS FULL

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ring nodes :
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chain bonds :
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    31-33
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exact/norm bonds :
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exact bonds :
    3-14  3-34  30-31
normalized bonds :
    19-20  19-24  20-21  21-22  22-23  23-24  23-25  24-28  25-26  26-27  27-28


Match level :
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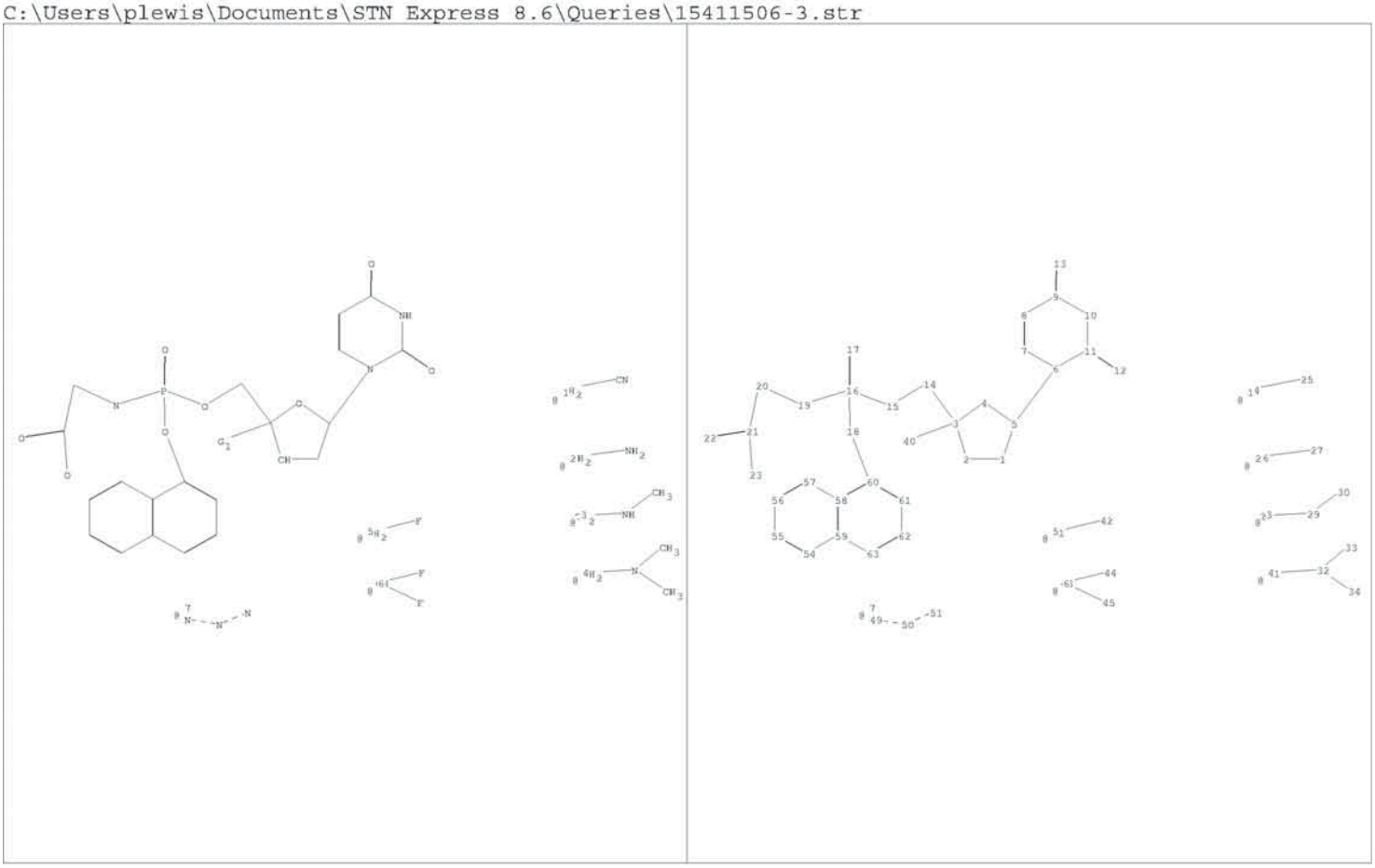
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L3           0 S L1 SSS FULL
L4             STRUCTURE UPLOADED
L5           0 S L4 SSS SAM
L6           0 S L4 SSS FULL
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C:\Users\plewis\Documents\STN Express 8.6\Queries\15411506-3.str



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ring bonds :
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exact/norm bonds :
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exact bonds :
    3-14  20-21  24-25  26-27  28-29  29-30  31-32  32-33  32-34  41-42  43-44  43-45
normalized bonds :
    54-55  54-59  55-56  56-57  57-58  58-59  58-60  59-63  60-61  61-62  62-63

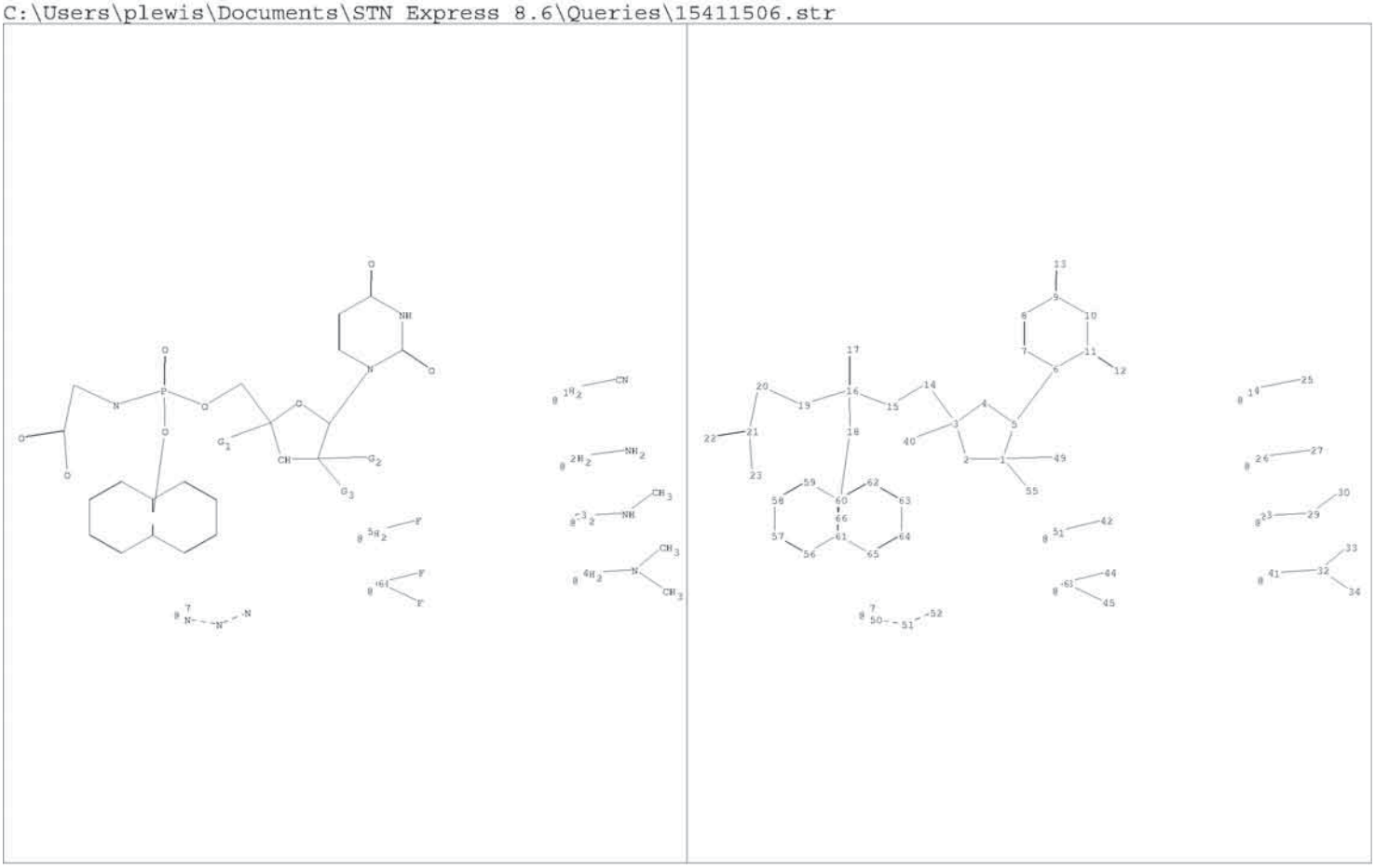

G1:[@1],[@2],[@3],[@4]

G2:H,CH3,CF3,CN,F,[@5],[@6]

G3:H,X,OH,MeO,NH2,[@7]

Match level :
    1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom  11:Atom
    12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS  19:CLASS  20:CLASS
    21:CLASS  22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS
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    44:CLASS  45:CLASS  49:CLASS  50:CLASS  51:CLASS  54:Atom  55:Atom  56:Atom  57:Atom  58:Atom
    59:Atom  60:Atom  61:Atom  62:Atom  63:Atom
```

C:\Users\plewis\Documents\STN Express 8.6\Queries\15411506.str



```
chain nodes :
    12  13  14  15  16  17  18  19  20  21  22  23  24  25  26  27  28  29  30  31  32  33  34  40
    41  42  43  44  45  49  50  51  52  55
ring nodes :
    1  2  3  4  5  6  7  8  9  10  11  56  57  58  59  60  61  62  63  64  65
chain bonds :
    1-49  1-55  3-14  3-40  5-6  9-13  11-12  14-15  15-16  16-17  16-18  16-19  19-20  20-21
    21-22  21-23  24-25  26-27  28-29  29-30  31-32  32-33  32-34  41-42  43-44  43-45  50-51
    51-52
ring bonds :
    1-2  1-5  2-3  3-4  4-5  6-7  6-11  7-8  8-9  9-10  10-11  56-57  56-61  57-58  58-59  59-60
    60-61  60-62  61-65  62-63  63-64  64-65
exact/norm bonds :
    1-2  1-5  1-49  1-55  2-3  3-4  3-40  4-5  5-6  6-7  6-11  7-8  8-9  9-10  9-13  10-11  11-12
    14-15  15-16  16-17  16-18  16-19  19-20  21-22  21-23  50-51  51-52
exact bonds :
    3-14  20-21  24-25  26-27  28-29  29-30  31-32  32-33  32-34  41-42  43-44  43-45
normalized bonds :
    56-57  56-61  57-58  58-59  59-60  60-61  60-62  61-65  62-63  63-64  64-65

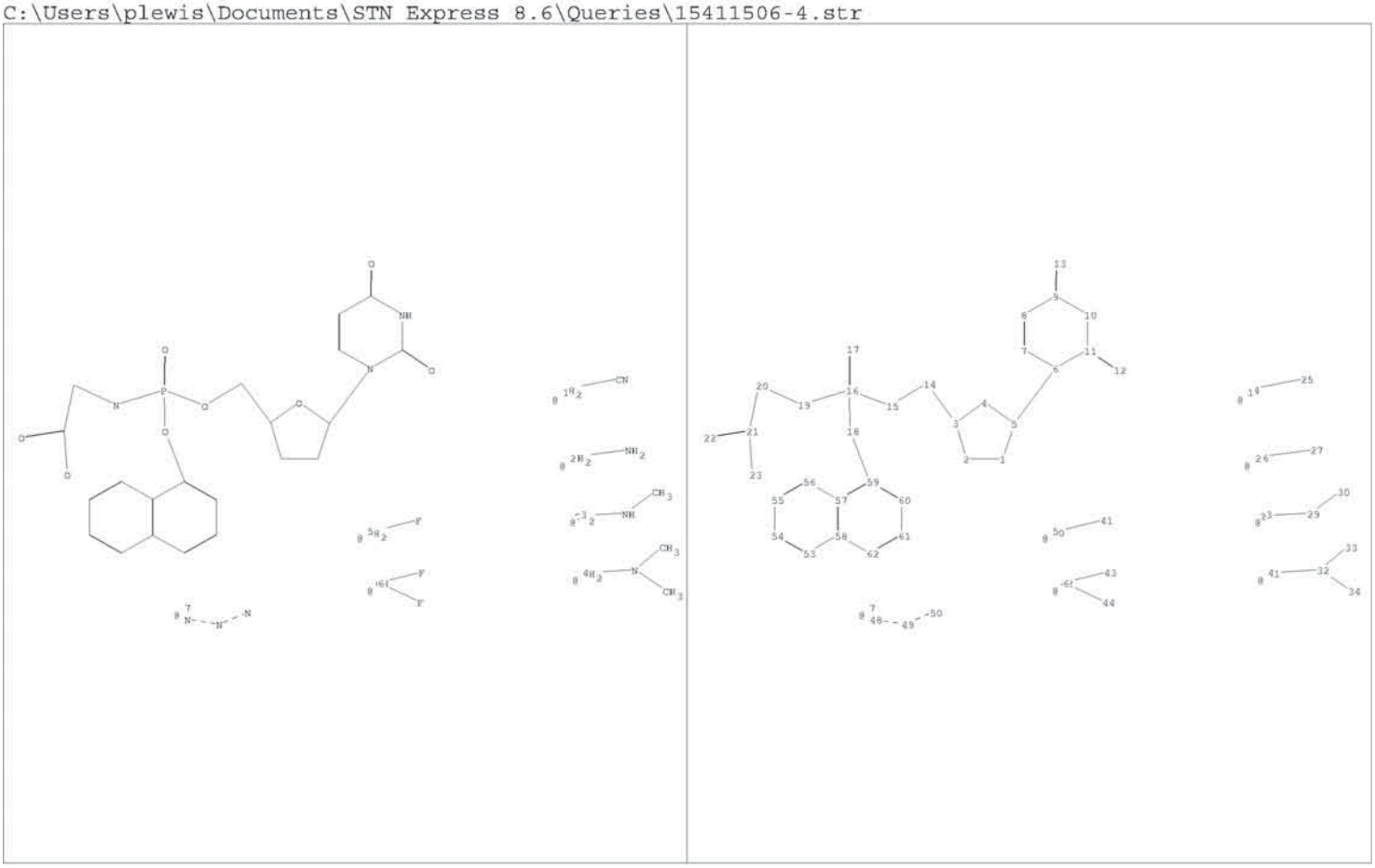

G1:[@1],[@2],[@3],[@4]

G2:H,CH3,CF3,CN,F,[@5],[@6]

G3:H,X,OH,MeO,NH2,[@7]

Match level :
    1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom  11:Atom
    12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS  19:CLASS  20:CLASS
    21:CLASS  22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS
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    59:Atom  60:Atom  61:Atom  62:Atom  63:Atom  64:Atom  65:Atom  66:CLASS
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C:\Users\plewis\Documents\STN Express 8.6\Queries\15411506-4.str



```
chain nodes :
    12  13  14  15  16  17  18  19  20  21  22  23  24  25  26  27  28  29  30  31  32  33  34  40
    41  42  43  44  48  49  50
ring nodes :
    1  2  3  4  5  6  7  8  9  10  11  53  54  55  56  57  58  59  60  61  62
chain bonds :
    3-14  5-6  9-13  11-12  14-15  15-16  16-17  16-18  16-19  18-59  19-20  20-21  21-22  21-23
    24-25  26-27  28-29  29-30  31-32  32-33  32-34  40-41  42-43  42-44  48-49  49-50
ring bonds :
    1-2  1-5  2-3  3-4  4-5  6-7  6-11  7-8  8-9  9-10  10-11  53-54  53-58  54-55  55-56  56-57
    57-58  57-59  58-62  59-60  60-61  61-62
exact/norm bonds :
    1-2  1-5  2-3  3-4  4-5  5-6  6-7  6-11  7-8  8-9  9-10  9-13  10-11  11-12  14-15  15-16
    16-17  16-18  16-19  18-59  19-20  21-22  21-23  48-49  49-50
exact bonds :
    3-14  20-21  24-25  26-27  28-29  29-30  31-32  32-33  32-34  40-41  42-43  42-44
normalized bonds :
    53-54  53-58  54-55  55-56  56-57  57-58  57-59  58-62  59-60  60-61  61-62


G1:[@1],[@2],[@3],[@4]

G2:H,CH3,CF3,CN,F,[@5],[@6]

G3:H,X,OH,MeO,NH2,[@7]

Match level :
    1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom  11:Atom
    12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS  19:CLASS  20:CLASS
    21:CLASS  22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS
    30:CLASS  31:CLASS  32:CLASS  33:CLASS  34:CLASS  40:CLASS  41:CLASS  42:CLASS  43:CLASS
    44:CLASS  48:CLASS  49:CLASS  50:CLASS  53:Atom  54:Atom  55:Atom  56:Atom  57:Atom  58:Atom
    59:Atom  60:Atom  61:Atom  62:Atom
```

Notice of References Cited	Application/Control No. 15/411,506	Applicant(s)/Patent Under Reexamination Du et al.	
	Examiner PATRICK T LEWIS	Art Unit 1673	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-6784166-B2	08-2004	Devos; Rene Robert	A61K31/52	514/263.4
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

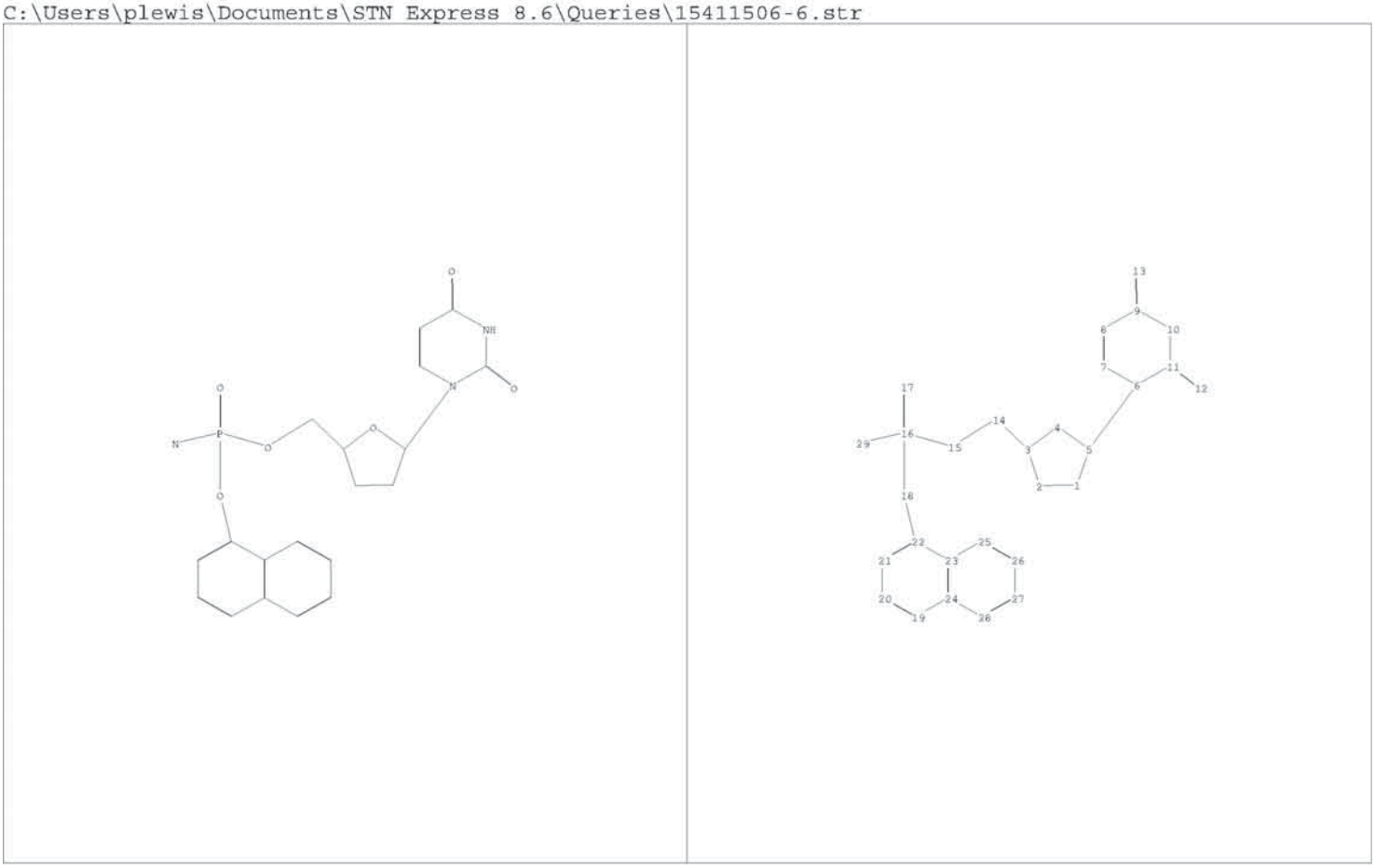
NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Congiatu et al. J. Med. Chem. (2006), Vol. 49, pages 452-455.
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Gilead Exhibit 2020
PGR2023-00046 - Page 00844

C:\Users\plewis\Documents\STN Express 8.6\Queries\15411506-6.str



```
chain nodes :
    12  13  14  15  16  17  18  29
ring nodes :
    1  2  3  4  5  6  7  8  9  10  11  19  20  21  22  23  24  25  26  27  28
chain bonds :
    3-14  5-6  9-13  11-12  14-15  15-16  16-17  16-18  16-29  18-22
ring bonds :
    1-2  1-5  2-3  3-4  4-5  6-7  6-11  7-8  8-9  9-10  10-11  19-20  19-24  20-21  21-22  22-23
    23-24  23-25  24-28  25-26  26-27  27-28
exact/norm bonds :
    1-2  1-5  2-3  3-4  4-5  5-6  6-7  6-11  7-8  8-9  9-10  9-13  10-11  11-12  14-15  15-16
    16-17  16-18  16-29  18-22
exact bonds :
    3-14
normalized bonds :
    19-20  19-24  20-21  21-22  22-23  23-24  23-25  24-28  25-26  26-27  27-28


Match level :
    1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom  11:Atom
    12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS  19:Atom  20:Atom  21:Atom
    22:Atom  23:Atom  24:Atom  25:Atom  26:Atom  27:Atom  28:Atom  29:CLASS
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WEST Search History

Hide Items | Restore | Clear | Close

DATE: Sunday, April 01, 2018

Hide?	Set Name	Query	Hit Count
Interference			
DB=PGPB,USPT; PLUR=YES; OP=ADJ			
☐	L10	L9 and 4 ' c	24
☐	L9	L8 and ns5a inhibitor	144
☐	L8	L7 and protease inhibitor	322
☐	L7	L6 and naphthyl	394
☐	L6	L5 and hcv	461
☐	L5	L4 and (uracil or uridine or $ uracil or $ uridine)	783
☐	L4	L3 and (prodrug or protide)	859
☐	L3	L2 and phosphoramidate	1501
☐	L2	L1 SPACE~or ((A61K31/7068 | A61K31/7072 | A61K31/706 | A61K31/7064 | C07H19/06 | C07H19/04 | C07H19/073).CPC.)	11670
☐	L1	514/42 or 514/43 or 514/49 or 514/50 or 514/51	5719

END OF SEARCH HISTORY

Gilead Exhibit 2020
PGR2023-00046 - Page 00846

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

117796 7590 04/09/2018

Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CALIFORNIA 94301
UNITED STATES OF AMERICA

EXAMINER
LEWIS, PATRICK T

ART UNIT	PAPER NUMBER
1673	

DATE MAILED: 04/09/2018

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/411,506	01/20/2017	Jinfa Du	37JD-199059-US9	9714

TITLE OF INVENTION: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
REGULAR	UNDISCOUNTED	$1000	$0.00	$0.00	$1000	07/09/2018

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

Gilead Exhibit 2020
PGR2023-00046 - Page 00847

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

117796 7590 04/09/2018

Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CALIFORNIA 94301
UNITED STATES OF AMERICA

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/411,506	01/20/2017	Jinfa Du	37JD-199059-US9	9714

TITLE OF INVENTION: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
REGULAR	UNDISCOUNTED	$1000	$0.00	$0.00	$1000	07/09/2018

EXAMINER	ART UNIT	CLASS-SUBCLASS
LEWIS, PATRICK T	1673	514-051000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29

❑ Applicant asserting small entity status. See 37 CFR 1.27

❑ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Gilead Exhibit 2020
PGR2023-00046 - Page 00848

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/411,506	01/20/2017	Jinfa Du	37JD-199059-US9	9714

117796 7590 04/09/2018

Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CALIFORNIA 94301
UNITED STATES OF AMERICA

EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1673	

DATE MAILED: 04/09/2018

PTOL-85 (Rev. 02/11)

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 15/411,506	Applicant(s) Du et al.	
	Examiner PATRICK T LEWIS	Art Unit 1673	AIA Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to Amendment dated 1/20/2017.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are 1-19 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file areply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☑ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☑ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/PATRICK T LEWIS/
Primary Examiner, Art Unit 1673

Gilead Exhibit 2020
PGR2023-00046 - Page 00851

Notice of Pre-AIA or AIA Status

1. The present application is being examined under the pre-AIA first to invent provisions.

EXAMINER'S AMENDMENT

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

3. The application has been amended as follows:

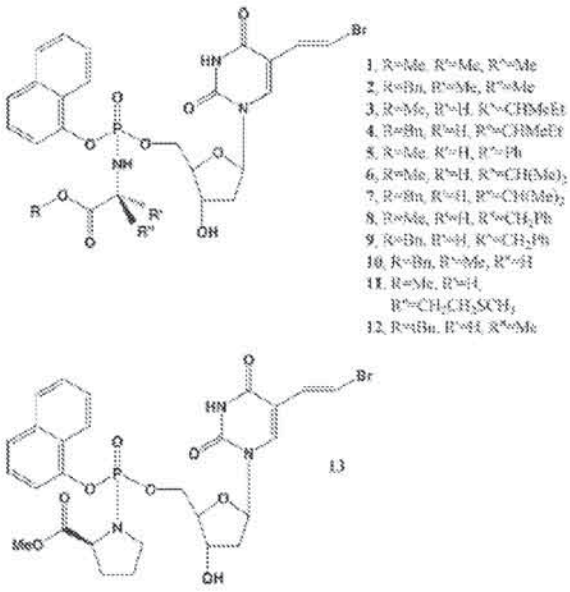
At the end of claim 1, the text "; and" has been deleted and a period ---.--- has been inserted therefor.

Allowable Subject Matter

4. The following is an examiner's statement of reasons for allowance: Congiatu et al. J. Med. Chem. (2006), Vol. 49, pages 452-455 (Congiatu) is representative of prior art. Congiatu teaches the preparation of a series of phenyl phosphoramidates related to thymectacin, tuning the phenyl, ester, and amino acid regions, observing significant enhancements in activity versus three different tumor cell lines (page 452). Because lipophilicity might play a crucial role for the delivery of ProTides inside cells, new analogues have been designed focusing on the introduction of naphthyl as new aromatic masking group on the phosphate moiety, which has led to a further increase in cytostatic activity against a panel of cancer cell lines. Compounds 1-13 were for their cytostatic

activity against a panel of different tumor cell lines in vitro: MDA MB231 (breast cancer) and PC-3 (prostate cancer) for entries 1-5 and thymectacin; T24 (bladder cancer) was also considered for entries 6-13. Data are reported in Table 1.

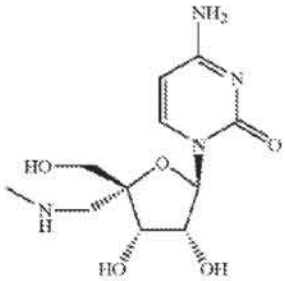
Scheme 1. Structures of 1−13



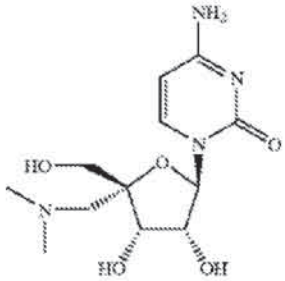
Congiatu differs from the instantly claimed invention in that Congiatu does not teach nor suggest a compound of instant formula IA wherein R^5 is CH_2CN, CH_2NH_2, CH_2NHCH_3, or $CH_2N(CH_3)_2$.

While 4'-substituted nucleosides, such as compounds **40** and **42** disclosed by Devos et al. US 6,784,166 B2 (Devos), were known at the time of the instant invention,

compound 40 4'-C-[(Methylamino)methyl]-cytidine



compound 42 4'-C-[(Dimethylamino)methyl]-cytidine



modification of the 5'-position of compound **40** or **42** with a naphthyl phosphoramidate of Congiatu would not yield a compound embraced by instant formula IA (different nucleobase and intended use).

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

5. Claims 1-19 are allowed.

Contacts

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PATRICK T LEWIS whose telephone number is (571)272-0655. The examiner can normally be reached on Monday to Friday, 10 AM to 4 PM EST (Maxi Flex).

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an

interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/PATRICK T LEWIS/
Primary Examiner, Art Unit 1673

/PL/

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/411,506	Du et al.
	Examiner	Art Unit
	PATRICK T LEWIS	1673

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

CLAIMS										
☑ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47										
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	19	=								

Gilead Exhibit 2020
PGR2023-00046 - Page 00856

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/411,506	Du et al.
	Examiner	Art Unit
	PATRICK T LEWIS	1673

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

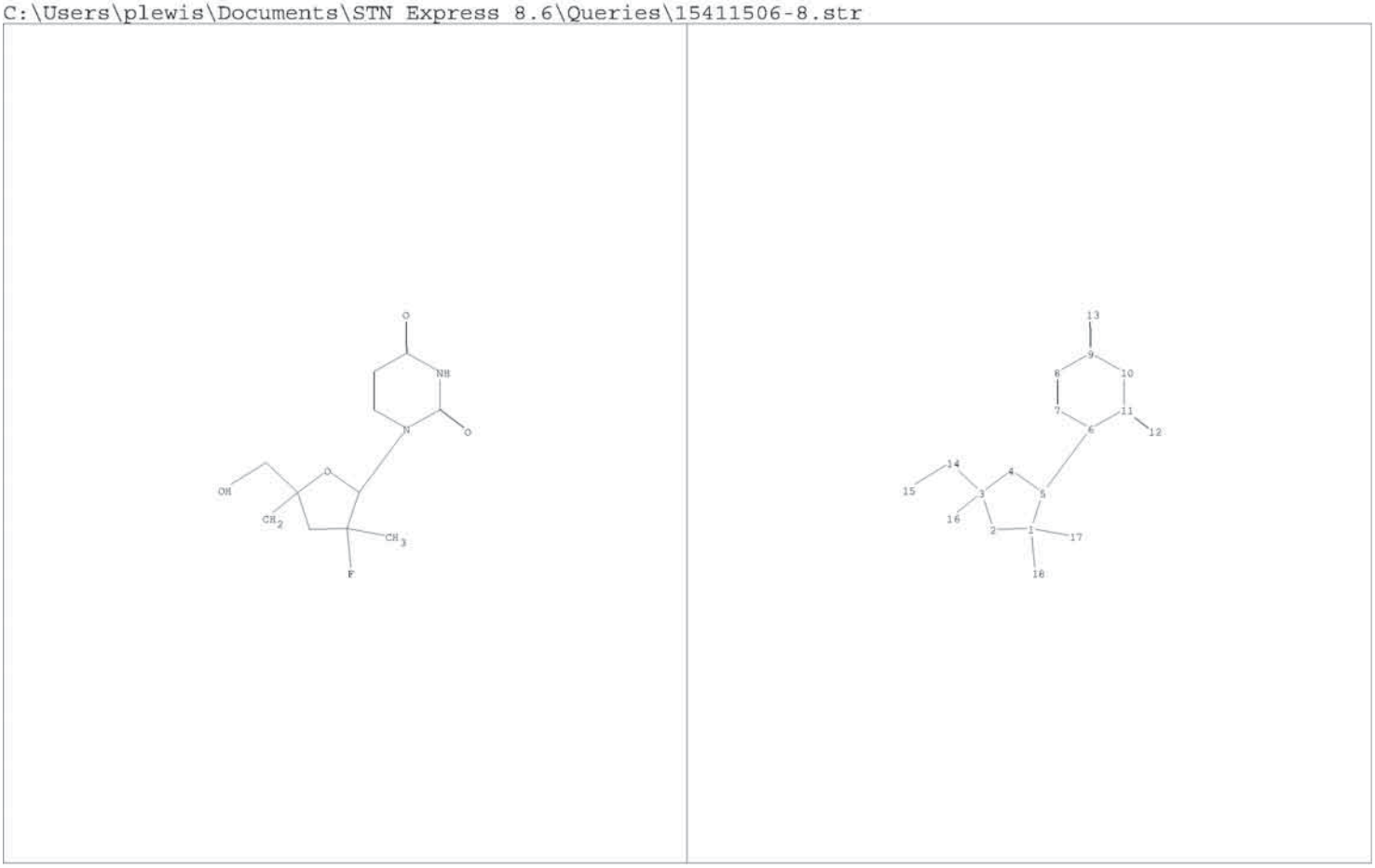
Search Notes		
Search Notes	Date	Examiner
Inventor, REGISTRY, CAPLUS, MEDLINE (see attached)	04/01/2018	/PL/

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
514	42, 43, 49, 50, 51	04/01/2018	/PL/
A61K	31/7068, 31/7072, 31/706, 31/7064	04/01/2018	/PL/
C07H	19/06, 19/073, 19/04	04/01/2018	/PL/

/PATRICK T LEWIS/ Primary Examiner, Art Unit 1673	

Gilead Exhibit 2020
PGR2023-00046 - Page 00857

C:\Users\plewis\Documents\STN Express 8.6\Queries\15411506-8.str




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exact/norm bonds :
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exact bonds :
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UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

BIB DATA SHEET

CONFIRMATION NO. 9714

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
15/411,506	01/20/2017	514	1673	PH3080.PC4C2

APPLICANTS

Gilead Pharmasset LLC, Foster City, CA;

INVENTORS

Jinfa Du, Redwood City, CA;
Dhanapalan Nagarathnam, Bethany, CT;
Michael Joseph Sofia, Doylestown, PA;
Peiyuan Wang, San Mateo, CA;

**** CONTINUING DATA ***************************

This application is a CON of 14/656,546 03/12/2015 PAT 9585906
which is a CON of 14/013,237 08/29/2013 PAT 9085573
which is a CON of 13/609,614 09/11/2012 PAT 8580765
which is a CON of 13/099,671 05/03/2011 PAT 8334270
which is a CON of 12/053,015 03/21/2008 PAT 7964580
which claims benefit of 60/982,309 10/24/2007
and claims benefit of 60/909,315 03/30/2007

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ****

01/30/2017

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☑ No Verified and Acknowledged /PATRICK T LEWIS/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		CA	0	19	1

ADDRESS

Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301
UNITED STATES

TITLE

NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

FILING FEE RECEIVED		
5740	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/411,506	Du et al.
	Examiner	Art Unit
	PATRICK T LEWIS	1673

CPC								
Symbol							Type	Version
A61K	/	31	/	7072			F	2013-01-01
C07H	/	19	/	06			I	2013-01-01
A61K	/	45	/	06			I	2013-01-01
C07H	/	19	/	04			A	2013-01-01
C07H	/	19	/	073			A	2013-01-01
A61K	/	31	/	7064			A	2013-01-01
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A61K	/	31	/	7068			A	2013-01-01

CPC Combination Sets								
Symbol							Type	Set	Ranking	Version
	/		/							

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(Assistant Examiner)	(Date)	19	
/PATRICK T LEWIS/ Primary Examiner, Art Unit 1673	01 April 2018	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

U.S. Patent and Trademark Office

Part of Paper No.: 20180401

Gilead Exhibit 2020
PGR2023-00046 - Page 00860

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/411,506	Du et al.
	Examiner	Art Unit
	PATRICK T LEWIS	1673

INTERNATIONAL CLASSIFICATION					
CLAIMED					
A01N	/	43	/	04	
A61K	/	31	/	70	

NON-CLAIMED					
	/		/		

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS
514	51

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					
514	42	43	49	50		

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	19	
/PATRICK T LEWIS/ Primary Examiner, Art Unit 1673	01 April 2018	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Gilead Exhibit 2020
PGR2023-00046 - Page 00861

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/411,506	Du et al.
	Examiner	Art Unit
	PATRICK T LEWIS	1673

☑ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIMS

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
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	8		17												
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NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	19	
/PATRICK T LEWIS/ Primary Examiner, Art Unit 1673	01 April 2018	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

U.S. Patent and Trademark Office

Part of Paper No.: 20180401

Gilead Exhibit 2020
PGR2023-00046 - Page 00862

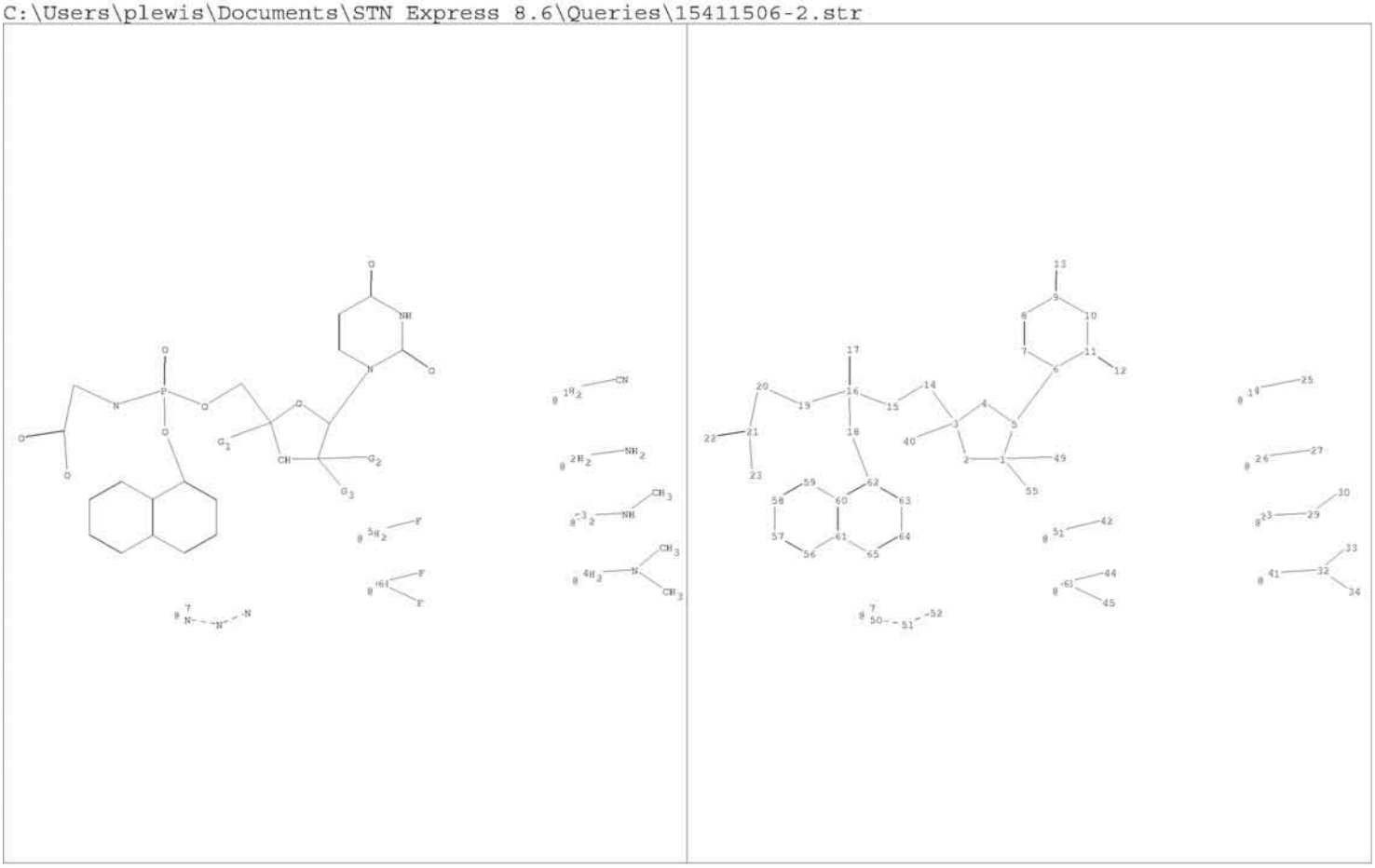
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G1:[@1],[@2],[@3],[@4]

G2:H,CH3,CF3,CN,F,[@5],[@6]

G3:H,X,OH,MeO,NH2,[@7]

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PTO/SB/30 (11-17)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Request for Continued Examination (RCE) Transmittal

Address to:
Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Application Number	15/411,506
Filing Date	January 20, 2017
First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO) on page 2.

1. Submission required under 37 CFR 1.114 Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).
   - a. ☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.
     - i. ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
     - ii. ☐ Other _____
   - b. ☒ Enclosed
     - i. ☐ Amendment/Reply
     - ii. ☐ Affidavit(s)/ Declaration(s)
     - iii. ☒ Information Disclosure Statement (IDS)
     - iv. ☐ Other _____
2. Miscellaneous
   - a. ☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)
   - b. ☐ Other _____
3. Fees The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.
   - a. ☒ The Director is hereby authorized to charge the following fees, any underpayment of fees, or credit any overpayments, to Deposit Account No. 50-4561 .
     - i. ☒ RCE fee required under 37 CFR 1.17(e)
     - ii. ☐ Extension of time fee (37 CFR 1.136 and 1.17)
     - iii. ☐ Other _____
   - b. ☐ Check in the amount of $ _____ enclosed
   - c. ☐ Payment by credit card (Form PTO-2038 enclosed)
   - d. ☒ Payment by EFS-Web

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Signature	/Neeta C. Thakur/	Date	July 6, 2018
Name (Print/Type)	Neeta C. Thakur	Registration No.	59,123

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being EFS-Web transmitted to the United States Patent and Trademark Office (USPTO), deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 or facsimile transmitted to the USPTO on the date shown below.

Signature	E-FILED		
Name (Print/Type)		Date	

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
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Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: July 6, 2018

(use as many sheets as necessary)

Sheet 1 of 38

Complete if Known	
Application Number	15/411,506
Filing Date	January 20 2017
First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Document Number Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	20010034440 A1	10/25/2001	Shepard et al.	
	A2	20020058635 A1	05/16/2002	Averett	
	A3	20020198173 A1	12/26/2002	Schinazi et al.	
	A4	20030050229 A1	03/13/2003	Sommadossi et al.	
	A5	20030060400 A1	03/27/2003	LaColla et al.	
	A6	20030109697 A1	07/12/2003	Shepard et al.	
	A7	20030120071 A1	06/26/2003	McGuigan et al.	
	A8	20030144502 A1	07/31/2003	Pietrzkowski et al.	
	A9	20030153744 A1	08/14/2003	Mekouar et al.	
	A10	20030187018 A1	10/02/2003	Llinas-Brunet et al.	
	A11	20040006007 A1	01/08/2004	Gosselin et al.	
	A12	20040014108 A1	01/22/2004	Eldrup et al.	
	A13	20040023240 A1	02/05/2004	Marliere et al.	
	A14	20040023901 A1	02/05/2004	Cook et al.	
	A15	20040059104 A1	03/25/2004	Cook et al.	
	A16	20040063622 A1	04/01/2004	Sommadossi et al.	
	A17	20040067901 A1	04/08/2004	Bhat et al.	
	A18	20040072788 A1	04/15/2004	Bhat et al.	
	A19	20040097461 A1	05/20/2004	Sommadossi et al.	
	A20	20040097462 A1	05/20/2004	Sommadossi et al.	
	A21	20040101535 A1	05/27/2004	Sommadossi et al.	
	A22	20040102414 A1	05/27/2004	Sommadossi et al.	
	A23	20040110717 A1	06/10/2004	Carroll et al.	
	A24	20040167140 A1	08/26/2004	Schinazi et al.	
	A25	20040191824 A1	09/30/2004	Dempcy et al.	
	A26	20040214844 A1	10/28/2004	Otto et al.	
	A27	20040229839 A1	11/18/2004	Babu et al.	
	A28	20040229840 A1	11/18/2004	Bhat et al.	
	A29	20040248892 A1	12/09/2004	Wang	
	A30	20040254141 A1	12/16/2004	Schinazi et al.	
	A31	20040259934 A1	12/23/2004	Olsen et al.	
	A32	20040265969 A1	12/30/2004	Li et al.	
	A33	20040266996 A1	12/30/2004	Rabi	
	A34	20050009737 A1	01/13/2005	Clark	
	A35	20050020825 A1	01/27/2005	Storer et al.	
	A36	20050026853 A1	02/03/2005	Mekouar et al.	

Examiner Signature		Date Considered	

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Date Submitted: July 6, 2018

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Sheet 2 of 38

Complete if Known	
Application Number	15/411,506
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First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Document Number Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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Sheet 3 of 38

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Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

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Sheet 4 of 38

Complete if Known	
Application Number	15/411,506
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First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

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Sheet 5 of 38

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Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: July 6, 2018

(use as many sheets as necessary)

Sheet 7 of 38

Complete if Known	
Application Number	15/411,506
Filing Date	January 20 2017
First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Document Number Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A217	6753309 B2	06/22/2004	Klecker et al.	
	A218	6777395 B2	08/17/2004	Bhat et al.	
	A219	6784166 B2	08/31/2004	Devos et al.	
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	A221	6787526 B1	09/07/2004	Bryant et al.	
	A222	6812219 A	11/02/2004	LaColla et al.	
	A223	6815542 B2	11/09/2004	Hong et al.	
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	A250	7754699 A	07/13/2010	Chun et al.	
	A251	7879815 B2	02/01/2011	MacCoss et al.	
	A252	7964580 B2	06/21/2011	Sofia et al.	

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Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	15/411,506
Date Submitted: July 6, 2018				Filing Date	January 20 2017
				First Named Inventor	Jinfa Du
				Art Unit	1673
(use as many sheets as necessary)				Examiner Name	Patrick T. Lewis
Sheet	8	of	38	Attorney Docket Number	37JD-199059-US9

U.S. PATENT DOCUMENTS					
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	A253	8148349 B2	04/03/2012	Meppen et al.	
	A254	8173621 B2	05/08/2012	Du et al.	
	A255	8334270 B2	12/18/2012	Sofia et al.	
	A256	8415322 B2	04/29/2013	Clark	
	A257	8551973 B2	10/08/2013	Bao et al.	
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UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
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First Named Inventor	Jinfa Du
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Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

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	A265	CN 101108870 A	01/23/2008	Yixin Leng		
	A266	DE 19914474 A1	10/07/1999	Hoffmann La Roche		
	A267	EP 0180276 A1	05/07/1986	Oce Andeno Bv		
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	A269	EP 1828217 A2	09/05/2007	FEBIT BIOTECH GMBH		
	A270	EP 1881001 A1	01/23/2008	TIBOTEC PHARM, LTD.		
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	A276	WO 1989/002733 A1	04/06/1989	Univ California;		
	A277	WO 1990/000555 A1	01/25/1990	Vical Inc;		
	A278	WO 1991/016920 A1	11/14/1991	Vical Inc;		
	A279	WO 1991/018914 A1	12/12/1991	Vical Inc;		
	A280	WO 1991/019721 A1	12/26/1991	Glazier Arnold;		
	A281	WO 1993/000910 A1	01/21/1993	Vical Inc;		
	A282	WO 1994/026273 A1	11/24/1994	Hostetler Karl Y;		
	A283	WO 1995/013090 A1	05/18/1995	Enzon Inc;		
	A284	WO 1995/024185 A1	09/14/1995	Isis Pharmaceuticals Inc;		
	A285	WO 1996/015132 A1	05/23/1996	Univ California;		
	A286	WO 1996/032403 A2	10/17/1996	Schering Ag;		
	A287	WO 1996/029336 A1	09/26/1996	Medical Research Council		
	A288	WO 1997/012033 A1	04/03/1997	UNIV EMORY		
	A289	WO 1997/036554 A1	10/09/1997	Viropharma Inc;		
	A290	WO 1998/016184 A2	04/23/1998	Icn Pharmaceuticals;		
	A291	WO 1998/017679 A1	04/30/1998	Vertex Pharma;		
	A292	WO 1998/022496 A2	05/28/1998	Hoffmann La Roche;		
	A293	WO 1999/007734 A2	02/18/1999	Boehringer Ingelheim Ca Ltd;		
	A294	WO 1999/015194 A1	04/01/1999	Schering Corp;		
	A295	WO 1999/032139 A1	07/01/1999	Enzon Inc;		
	A296	WO 1999/032140 A1	07/01/1999	Enzon Inc;		
	A297	WO 1999/037753 A1	07/29/1999	Newbiotics, Inc.		

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Sheet 10 of 38

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Application Number	15/411,506
Filing Date	January 20 2017
First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

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	A299	WO 1999/059621 A1	11/25/1999	Schering Corp;		
	A300	WO 1999/064016 A1	12/16/1999	Hoffmann La Roche;		
	A301	WO 2000/006529 A1	02/10/2000	Angeletti P Ist Richerche Bio;		
	A302	WO 2000/009531 A2	02/24/2000	Novirio Pharmaceuticals Limite Centre Nat Rech Scient;		
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	A304	WO 2001/032153 A2	05/10/2001	Iaf Biochem Int;		
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	A306	WO 2001/007454 A1	02/01/2011	Newbiotics, Inc.		
	A307	WO 2001/079246 A2	10/25/2001	Pharmasset Ltd;		
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	A310	WO 2001/091737 A2	12/06/2001	Novirio Pharmaceuticals Ltd;		
	A311	WO 2001/092282 A2	12/06/2001	Novirio Pharmaceuticals Ltd; Univ Cagliari;		
	A312	WO 2001/096353 A2	12/20/2001	Novirio Pharmaceuticals Ltd; Ct Nat Da La Rech Scient Cnrs;		
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	A316	WO 2002/008251 A2	01/31/2002	Corvas Int Inc;		
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	A318	WO 2002/018404 A2	03/07/2002	Hoffmann La Roche;		
	A319	WO 2002/032414 A2	04/25/2002	Schering Corp; Albrecht Janice;		
	A320	WO 2002/032920 A2	04/25/2002	Pharmasset Ltd;		
	A321	WO 2002/048116 A2	06/20/2002	Bristol Myers Squibb Pharma Co;		
	A322	WO 2002/048157 A2	06/20/2002	Bristol Myers Squibb Pharma Co;		

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Sheet 11 of 38

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	A336	WO 2003/051899 A1	06/26/2003	RIBAPHARM INC.		
	A337	WO 2003/053989 A1	07/03/2003	MRC TECHNOLOGY LTD.		
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	A340	WO 2003/064456 A1	08/07/2003	BOEHRINGER INGELHEIM INT		
	A341	WO 2003/068244 A1	08/21/2003	Merck & Co Inc; Isis Pharmaceuticals Inc;		
	A342	WO 2003/101993 A1	12/11/2003	Neogenesis Pharmaceuticals Inc;		
	A343	WO 2003/104250 A1	12/18/2003	KYLIX B V		
	A344	WO 2003/105770 A2	12/24/2003	Merck & Co Inc;		
	A345	WO 2003/106477 A1	12/24/2003	Isis Pharmaceuticals Inc;		
	A346	WO 2004/000858 A2	12/31/2003	Merck & Co Inc; Isis Pharmaceuticals Inc;		
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	A350	WO 2004/002977 A1	01/08/2004	PHARMACIA & UPJOHN CO.		
	A351	WO 2004/002999 A2	01/08/2004	Idenix Cayman Ltd; Centre Nat Rech Scient; Univ Cagliari;		
	A352	WO 2004/003000 A2	01/08/2004	Idenix Cayman Ltd, Centre Nat Rech Scient; Univ Cagliari;		
	A353	WO 2004/003138 A2	01/08/2004	Merck & Co Inc; Isis Pharmaceuticals Inc;		
	A354	WO 2004/007512 A2	01/22/2004	Merck & Co Inc; Isis Pharmaceuticals Inc;		
	A355	WO 2004/009020 A2	01/29/2004	Merck & Co Inc; Isis Pharmaceuticals Inc;		
	A356	WO 2004/009610 A2	01/29/2004	Ptc Therapeutics Inc; Tularik Inc;		
	A357	WO 2004/011478 A2	02/05/2004	Micrologix Biotech Inc;		
	A358	WO 2004/014313 A2	02/19/2004	Squibb Bristol Myers Co;		
	A359	WO 2004/014852 A2	02/19/2004	Squibb Bristol Myers Co; Romine Jeffrey Lee		
	A360	WO 2004/035571 A1	04/29/2004	Rigel Pharmaceuticals Inc;		
	A361	WO 2004/041201 A2	05/21/2004	VIROPHARMA INC [US] WYETH CORP.		
	A362	WO 2004/046331 A2	06/03/2004	Idenix Cayman Ltd; Univ Cagliari;		
	A363	WO 2004/065367 A1	08/05/2004	BOEHRINGER INGELHEIM INT		
	A364	WO 2004/080466 A1	09/23/2004	Ribapharm Inc;		
	A365	WO 2004/094452 A2	11/04/2004	SQUIBB BRISTOL MYERS CO.		
	A366	WO 2004/096210 A1	11/11/2004	GLAXO GROUP L TO.		
	A367	WO 2004/096234 A2	11/11/2004	Gilead Sciences Inc;		
	A368	WO 2004/096235 A2	11/11/2004	Gilead Sciences Inc;		

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: July 6, 2018

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Sheet 13 of 38

Complete if Known	
Application Number	15/411,506
Filing Date	January 20 2017
First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

FOREIGN PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Foreign Patent Document Country Code[3]-Number[4]-Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	A369	WO 2004/096286 A2	11/11/2004	Gilead Sciences Inc		
	A370	WO 2004/106356 A1	12/09/2004	Univ Syddansk;		
	A371	WO 2005/002626 A2	01/13/2005	Gilead Sciences Inc;		
	A372	WO 2005/003147 A2	01/13/2005	Pharmasset Ltd;		
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	A374	WO 2005/009418 A2	02/03/2005	Idenix Cayman Ltd; Centre Nat Rech Scient;		
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	A381	WO 2005/067900 A2	07/28/2005	Achillion Pharmaceuticals Inc;		
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	A384	WO 2005/087788 A2	09/22/2005	Univ California;		
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	A389	WO 2006/012078 A2	02/02/2006	Merck & Co Inc;		
	A390	WO 2006/012440 A2	02/02/2006	Pharmasset Inc;		
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	A393	WO 2006/031725 A2	03/23/2006	Pharmasset Inc;		
	A394	WO 2006/035061 A1	04/06/2006	Tibotec Pharm Ltd;		
	A395	WO 2006/037028 A2	04/06/2006	Idenix Cayman Ltd; Centre Nat Rech Scient;		

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: July 6, 2018

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Sheet 14 of 38

Complete if Known	
Application Number	15/411,506
Filing Date	January 20 2017
First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

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	A397	WO 2006/063149 A1	06/15/2006	UNIV. MINNESOTA		
	A398	WO 2006/063717 A2	06/22/2006	UNIV. KARLSRUHE		
	A399	WO 2006/065335 A2	06/22/2006	Merck & Co Inc;		
	A400	WO 2006/065590 A2	06/22/2006	XTL BIOPHARMACEUTICALS INC.		
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	A402	WO 2006/093801 A1	09/08/2006	ABBOTT LAB		
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	A404	WO 2006/116557 A1	11/02/2006	GENELABS TECHNOLOGIES, INC.		
	A405	WO 2006/120251 A1	11/16/2006	Tibotec Pharm Ltd;		
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	A408	WO 2007/002602 A2	01/04/2007	DEPUY SPINE INC.		
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	A413	WO 2007/014926 A1	02/08/2007	TIBOTEC PHARM., LTD.		
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	A424	WO 2007/093901 A1	08/23/2007	PFIZER LTD.		
	A425	WO 2007/095269 A2	08/23/2007	MERCK & CO., INC.		
	A426	WO 2008/010921 A2	01/24/2008	GILEAD SCIENCES INC.		

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: July 6, 2018

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Sheet 15 of 38

Complete if Known	
Application Number	15/411,506
Filing Date	January 20 2017
First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

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	A428	WO 2008/048128 A1	04/24/2008	CT BADAN MOLEKULAR I MAKRO		
	A429	WO 2008/062206 A2	05/29/2008	UNIV. COLLEGE CARDIFF CONSULTANTS LTD.		
	A430	WO 2008/079206 A2	07/03/2008	MERCK & CO., INC.		
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	A437	WO 2009/120878 A2	10/01/2009	ALNYLAM PHARMACEUTICALS INC.		
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	A441	WO 2010/042834 A1	04/15/2010	Anadys Pharmaceuicals Inc.		
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	A444	WO 2011/123645 A2	10/06/2011	Pharmasset, Inc.		

NON PATENT LITERATURE DOCUMENTS

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	A446	ABRAHAM et al., "Synthesis, Biological Activity and Decomposition Studies of Amino Acid Phosphomonoester Amidates of Acyclovir," Nucleosides, Nucleotides and Nucleic Acids, vol. 16, No. 10, pp. 2079-2092 (1997).	

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Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	15/411,506
				Filing Date	January 20 2017
Date Submitted: July 6, 2018				First Named Inventor	Jinfa Du
				Art Unit	1673
(use as many sheets as necessary)				Examiner Name	Patrick T. Lewis
Sheet	16	of	38	Attorney Docket Number	37JD-199059-US9

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	A461	BEAULIEU et al., "Inhibitors of the HCV NS5B polymerase: New hope for the treatment of hepatitis C infections," Current Opinion in Investigational Drugs, vol. 5, No. 8, pp. 838-850 (2004).	
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Sheet 18 of 38

Complete if Known	
Application Number	15/411,506
Filing Date	January 20 2017
First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

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Examiner Name	Patrick T. Lewis
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Date Submitted: July 6, 2018

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Sheet 23 of 38

Complete if Known	
Application Number	15/411,506
Filing Date	January 20 2017
First Named Inventor	Jinfa Du
Art Unit	1673
Examiner Name	Patrick T. Lewis
Attorney Docket Number	37JD-199059-US9

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