R^5 is H, $C(=O)R^{1c}$, $C(=O)R^{1b}$, $P(=O)(OR^1)(OR^{1a})$, or $P(=O)(OR^1)(NR^4R^7)$;

R^6 is OH or F;

R^7 is $C(R^{2a}R^{2b})C(=O)OR^3$

m is 0 to 3;

n is 3, 4 or 5;

p is 0 to 2;

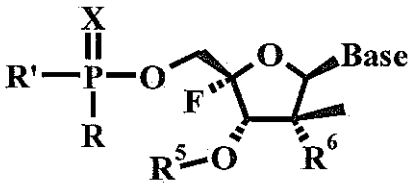
r is 1 to 6;

X is O or S; and

Base is uracil, cytosine, guanine, adenine, thymine, or heterocycloalkyl, each of which may optionally substituted with one or more hydroxy, lower alkyl, lower alkoxy, halo, nitro or cyano;

or a pharmacologically acceptable salt thereof.

[0006a] In one aspect, there is provided a compound of Formula I



I

wherein:

R is $O\text{-}R^1$ or $NHR^{1'}$;

or R and R^5 together form a bond;

R' is $N(R^4)C(R^{2a})(R^{2b})C(=O)OR^3$ or –O- C_1-C_7 alkyl;

R^1 is aryl, wherein aryl is phenyl or naphthyl, optionally substituted with one or more C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_1-C_7 alkoxy, halo, C_1-C_7 haloalkyl, $-N(R^{1a})_2$, acylamino, $-SO_2N(R^{1a})_2$, $-COR^{1b}$, $-SO_2(R^{1c})$, $-NHSO_2(R^{1c})$, nitro or cyano;

each R^{1a} is independently H or C_1-C_7 alkyl;

each R^{1b} is independently $-OR^{1a}$ or $-N(R^{1a})_2$;

each R^{1c} is C_1-C_7 alkyl;

$R^{1'}$ is $-C(R^{2a})(R^{2b})C(=O)OR^3$;

each R^{2a} and R^{2b} are independently H, C_1-C_7 alkyl, -$(CH_2)_rN(R^{1a})_2$, hydroxy-C_1-C_7-alkyl, -CH_2SH, -$(CH_2)S(O)_pMe$, -$(CH_2)_3NHC(=NH)NH_2$, (1*H*-indol-3-yl)methyl, (1*H*-indol-4-yl)methyl, -$(CH2)_mC(=O)R^{1b}$, aryl and aryl C_1-C_7 alkyl, wherein aryl may optionally be substituted with one or more hydroxy, C_1-C_7 alkyl, C_1-C_7 alkoxy, halo, nitro or cyano;

or R^{2a} is H;

each R^3 is H, C_1-C_7 alkyl, C_1-C_7 haloalkyl, phenyl or phenyl C_1-C_7 alkyl;

each R^4 is H, or C_1-C_7 alkyl;

R^5 is H;

R^6 is OH or F;

R^7 is $C(R^{2a}R^{2b})C(=O)OR^3$

m is 0 to 3;

n is 3, 4 or 5;

p is 0 to 2;

r is 1 to 6;

X is O or S; and

Base is cytosine, which may optionally substituted with one or more hydroxy, C_1-C_7 alkyl, C_1-C_7 alkoxy, halo, nitro or cyano;

wherein R' is –O- C_1-C_7 alkyl when R and R^5 together form a bond;

or a pharmacologically acceptable salt thereof.

[0006b] In another aspect, there is provided a compound selected from the group consisting of:

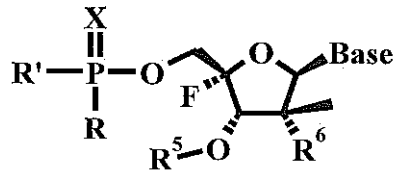
2'-Deoxy-2',4'-difluoro-2'-methycytidine-5'-(*O*-phenyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiosphosphoramidate;

2'-Deoxy-2',4'-difluoro-2'-methylcytidine-5'-(*O*-1-naphthyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiosphosphoramidate;

2'-Deoxy-2',4'-difluoro-2'-methylcytidine-5'-(*O*-2-naphthyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiosphosphoramidate;

WE CLAIM:

1. A compound of Formula I



I

wherein:

R is O-R^1 or $NHR^{1'}$;

or R and R^5 together form a bond;

R' is $N(R^4)C(R^{2a})(R^{2b})C(=O)OR^3$ or –O- C_1-C_7 alkyl;

R^1 is aryl, wherein aryl is phenyl or naphthyl, optionally substituted with one or more C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_1-C_7 alkoxy, halo, C_1-C_7 haloalkyl, $-N(R^{1a})_2$, acylamino, $-SO_2N(R^{1a})_2$, $-COR^{1b}$, $-SO_2(R^{1c})$, $-NHSO_2(R^{1c})$, nitro or cyano;

each R^{1a} is independently H or C_1-C_7 alkyl;

each R^{1b} is independently $-OR^{1a}$ or $-N(R^{1a})_2$;

each R^{1c} is C_1-C_7 alkyl;

$R^{1'}$ is $-C(R^{2a})(R^{2b})C(=O)OR^3$;

each R^{2a} and R^{2b} are independently H, C_1-C_7 alkyl, $-(CH_2)_rN(R^{1a})_2$, hydroxy-C_1-C_7-alkyl, $-CH_2SH$, $-(CH_2)S(O)_pMe$, $-(CH_2)_3NHC(=NH)NH_2$, (1*H*-indol-3-yl)methyl, (1*H*-indol-4-yl)methyl, $-(CH2)_mC(=O)R^{1b}$, aryl and aryl C_1-C_7 alkyl, wherein aryl may optionally be substituted with one or more hydroxy, C_1-C_7 alkyl, C_1-C_7 alkoxy, halo, nitro or cyano;

or R^{2a} is H;

each R^3 is H, C_1-C_7 alkyl, C_1-C_7 haloalkyl, phenyl or phenyl C_1-C_7 alkyl;

each R^4 is H, or C_1-C_7 alkyl;

R^5 is H;

R^6 is OH or F;

R^7 is $C(R^{2a}R^{2b})C(=O)OR^3$

m is 0 to 3;

n is 3, 4 or 5;

p is 0 to 2;

r is 1 to 6;

X is O or S; and

Base is cytosine, which may optionally substituted with one or more hydroxy, C_1-C_7 alkyl, C_1-C_7 alkoxy, halo, nitro or cyano;

wherein R' is –O- C_1-C_7 alkyl when R and R^5 together form a bond;

or a pharmacologically acceptable salt thereof.

2. The compound of claim 1, wherein R^4 is H.

3. The compound of claim 2, wherein R^1 is naphthyl or phenyl.

4. The compound of claim 3, wherein R^{2a} is H.

5. The compound of claim 4, wherein R^{2b} is methyl.

6. The compound of claim 5, wherein R^3 is isopropyl.

7. The compound of claim 6, wherein R^5 is H.

8. The compound of claim 1, wherein R and R^5 together form a bond.

9. The compound of claim 8, wherein R^6 is OH.

10. The compound of claim 9, wherein R' is –O-isopropyl.

11. The compound of claim 1, wherein X is S.

12. A compound selected from the group consisting of:

2'-Deoxy-2',4'-difluoro-2'-methycytidine-5'-(*O*-phenyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiosphosphoramidate;

2'-Deoxy-2',4'-difluoro-2'-methylcytidine-5'-(*O*-1-naphthyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiosphosphoramidate;

2'-Deoxy-2',4'-difluoro-2'-methylcytidine-5'-(*O*-2-naphthyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiosphosphoramidate;

2'-Deoxy-2',4'-difluoro-2'-methylcytidine-3',5'-cyclic phosphoric acid isopropyl ester;

2'-Deoxy-2',4'-difluoro-2'-methylcytidine-3',5'-cyclic thiophosphoric acid isopropyl ester;

4'-Fluoro-2'-methylcytidine-5'-(*O*-phenyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl phosphoramidate;

4'-Fluoro-2'-cytidine-5'-(*O*-1-naphthyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl phosphoramidate;

4'-Fluoro-2'-methylcytidine-5'-(*O*-1-naphthyl-*N*-(S)-2-(isopropoxycarbonyl)ethyl phosphoramidate;

4'-Fluoro-2'-methylcytidine-5'-(*O*-phenyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiophsphoramidate;

4'-Fluoro-2'-methylcytidine-5'-(*O*-1-naphthyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiophosphoramidate;

4'-Fluoro-2'-methylcytidine-5'-(*O*-1-naphthyl-*N*-(S)-2-(isopropoxycarbonyl)ethyl thiophosphoramidate;

4'-Fluoro-2'-methylcytidine-3',5'-cyclic phosphoric acid isopropyl ester;

4'-Fluoro-2'-methylcytidine-3',5'-cyclic thiophosphoric acid isopropyl ester;

2'-Deoxy-2',4'-difluoro-2'-methylcytidine-5'-{*N,N'*-bis[(S)-1-(isopropoxylcarbonyl)ethyl]phosphorodiamidate;

2'-Deoxy-2',4'-difluoro-2'-methylcytidine-5'-{*N,N'*-bis[(S)-1-(isopropoxylcarbonyl)ethyl]thiophosphorodiamidate;

4'-Fluoro-2'-methylcytidine-5'-{*N,N'*-bis[(S)-1-(isopropoxylcarbonyl)ethyl]phosphorodiamidate; and

4'-Fluoro-2'-methylcytidine-5'-{*N,N'*-bis[(S)-1-(isopropoxylcarbonyl)ethyl]thiophosphorodiamidate.

13. A compound of claim 1 for use in the treatment of a Hepatitis C Virus (HCV) infection.

14. A combination of a compound of claim 1 with an immune system modulator and/or an antiviral agent that inhibits replication of HCV for use in the treatment of a Hepatitis C Virus (HCV) infection.

15. The combination of claim 14, wherein the immune system modulator is an interferon or chemically derivatized interferon.

16. The combination of claim 14, wherein the antiviral agent is selected from the group consisting of a HCV protease inhibitor, a HCV polymerase inhibitor, a HCV helicase inhibitor, a HCV primase inhibitor, a HCV fusion inhibitor, and a combination thereof.

17. Use of compound of claim 1 in the manufacture of a medicament for the treatment of a Hepatitis C Virus (HCV) infection.

18. The use of claim 17, further comprising an immune system modulator or an antiviral agent that inhibits replication of HCV, or a combination thereof.

19. The use according to claim 18, wherein the immune system modulator is an interferon or chemically derivatized interferon.

20. The use according to claim 18, wherein the antiviral agent is selected from the group consisting of a HCV protease inhibitor, a HCV polymerase inhibitor, a HCV helicase inhibitor, a HCV primase inhibitor, a HCV fusion inhibitor, and a combination thereof.

21. A compound of claim 1 for use in inhibiting replication of HCV in a cell.

22. Use of a compound of claim 1 in the manufacture of a medicament for the inhibition of replication of HCV in a cell.

23. A composition comprising the compound of claim 1, admixed with at least one carrier, diluent or excipient.