

Table XXXI-6.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-6-1	p-Me-Ph	H	H	H	CH ₃	H	F	F	OH
XXXI-6-2	p-Me-Ph	H	H	CH ₃	CH ₃	H	F	F	OH
XXXI-6-3	p-Me-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-6-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-6-5	p-Me-Ph	H	H	CH ₂ Ph	CH ₃	H	F	F	OH
XXXI-6-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	F	F	OH
XXXI-6-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	F	F	OH
XXXI-6-8	p-Me-Ph	*	H	*	CH ₃	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-7.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-7-1	p-F-Ph	H	H	H	CH ₃	H	F	F	OH
XXXI-7-2	p-F-Ph	H	H	CH ₃	CH ₃	H	F	F	OH
XXXI-7-3	p-F-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-7-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-7-6	p-F-Ph	H	H	CH ₂ Ph	CH ₃	H	F	F	OH
XXXI-7-7	p-F-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	F	F	OH
XXXI-7-8	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	F	F	OH
XXXI-7-20	p-F-Ph	*	H	*	CH ₃	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-8.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-8-1	p-Cl-Ph	H	H	H	CH ₃	H	F	F	OH
XXXI-8-2	p-Cl-Ph	H	H	CH ₃	CH ₃	H	F	F	OH
XXXI-8-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-8-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-8-5	p-Cl-Ph	H	H	CH ₂ Ph	CH ₃	H	F	F	OH
XXXI-8-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	F	F	OH
XXXI-8-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	F	F	OH
XXXI-8-8	p-Cl-Ph	*	H	*	CH ₃	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-9.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-9-1	p-Br-Ph	H	H	H	CH ₃	H	F	F	OH
XXXI-9-2	p-Br-Ph	H	H	CH ₃	CH ₃	H	F	F	OH
XXXI-9-3	p-Br-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-9-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-9-6	p-Br-Ph	H	H	CH ₂ Ph	CH ₃	H	F	F	OH
XXXI-9-7	p-Br-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	F	F	OH
XXXI-9-8	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	F	F	OH
XXXI-9-20	p-Br-Ph	*	H	*	CH ₃	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-10.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-10-1	p-I-Ph	H	H	H	CH ₃	H	F	F	OH
XXXI-10-2	p-I-Ph	H	H	CH ₃	CH ₃	H	F	F	OH
XXXI-10-3	p-I-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-10-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	F	F	OH
XXXI-10-5	p-I-Ph	H	H	CH ₂ Ph	CH ₃	H	F	F	OH
XXXI-10-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	F	F	OH
XXXI-10-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	F	F	OH
XXXI-10-8	p-I-Ph	*	H	*	CH ₃	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-11.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-11-1	CH ₃	H	H	H	Et	H	F	F	OH
XXXI-11-2	CH ₃	H	H	CH ₃	Et	H	F	F	OH
XXXI-11-3	CH ₃	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-11-4	CH ₃	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-11-5	CH ₃	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-11-6	CH ₃	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-11-7	CH ₃	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-11-8	CH ₃	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-12.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-12-1	Et	H	H	H	Et	H	F	F	OH
XXXI-12-2	Et	H	H	CH ₃	Et	H	F	F	OH
XXXI-12-3	Et	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-12-4	Et	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-12-5	Et	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-12-6	Et	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-12-7	Et	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-12-8	Et	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-13.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-13-1	ⁱ Pr	H	H	H	Et	H	F	F	OH
XXXI-13-2	ⁱ Pr	H	H	CH ₃	Et	H	F	F	OH
XXXI-13-3	ⁱ Pr	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-13-4	ⁱ Pr	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-13-5	ⁱ Pr	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-13-6	ⁱ Pr	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-13-7	ⁱ Pr	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-13-8	ⁱ Pr	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-14.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-14-1	^t Bu	H	H	H	Et	H	F	F	OH
XXXI-14-2	^t Bu	H	H	CH ₃	Et	H	F	F	OH
XXXI-14-3	^t Bu	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-14-4	^t Bu	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-14-5	^t Bu	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-14-6	^t Bu	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-14-7	^t Bu	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-14-8	^t Bu	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-15.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-15-1	Ph	H	H	H	Et	H	F	F	OH
XXXI-15-2	Ph	H	H	CH ₃	Et	H	F	F	OH
XXXI-15-3	Ph	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-15-4	Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-15-5	Ph	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-15-6	Ph	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-15-7	Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-15-8	Ph	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-16.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-16-1	p-Me-Ph	H	H	H	Et	H	F	F	OH
XXXI-16-2	p-Me-Ph	H	H	CH ₃	Et	H	F	F	OH
XXXI-16-3	p-Me-Ph	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-16-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-16-5	p-Me-Ph	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-16-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-16-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-16-8	p-Me-Ph	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-17.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-17-1	p-F-Ph	H	H	H	Et	H	F	F	OH
XXXI-17-2	p-F-Ph	H	H	CH ₃	Et	H	F	F	OH
XXXI-17-3	p-F-Ph	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-17-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-17-5	p-F-Ph	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-17-6	p-F-Ph	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-17-7	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-17-8	p-F-Ph	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-18.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-18-1	p-Cl-Ph	H	H	H	Et	H	F	F	OH
XXXI-18-2	p-Cl-Ph	H	H	CH ₃	Et	H	F	F	OH
XXXI-18-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-18-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-18-5	p-Cl-Ph	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-18-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-18-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-18-8	p-Cl-Ph	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-19.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-19-1	p-Br-Ph	H	H	H	Et	H	F	F	OH
XXXI-19-2	p-Br-Ph	H	H	CH ₃	Et	H	F	F	OH
XXXI-19-3	p-Br-Ph	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-19-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-19-5	p-Br-Ph	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-19-6	p-Br-Ph	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-19-7	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-19-8	p-Br-Ph	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-20.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-20-1	p-I-Ph	H	H	H	Et	H	F	F	OH
XXXI-20-2	p-I-Ph	H	H	CH ₃	Et	H	F	F	OH
XXXI-20-3	p-I-Ph	H	H	CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-20-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	F	F	OH
XXXI-20-5	p-I-Ph	H	H	CH ₂ Ph	Et	H	F	F	OH
XXXI-20-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	Et	H	F	F	OH
XXXI-20-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	F	F	OH
XXXI-20-8	p-I-Ph	*	H	*	Et	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-21.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-21-1	CH ₃	H	H	H	ⁱ Pr	H	F	F	OH
XXXI-21-2	CH ₃	H	H	CH ₃	ⁱ Pr	H	F	F	OH
XXXI-21-3	CH ₃	H	H	CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-21-4	CH ₃	H	H	CH ₂ CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-21-5	CH ₃	H	H	CH ₂ Ph	ⁱ Pr	H	F	F	OH
XXXI-21-6	CH ₃	H	H	CH ₂ -indol-3-yl	ⁱ Pr	H	F	F	OH
XXXI-21-7	CH ₃	H	H	CH ₂ CH ₂ SCH ₃	ⁱ Pr	H	F	F	OH
XXXI-21-8	CH ₃	*	H	*	ⁱ Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-22.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-22-1	Et	H	H	H	ⁱ Pr	H	F	F	OH
XXXI-22-2	Et	H	H	CH ₃	ⁱ Pr	H	F	F	OH
XXXI-22-3	Et	H	H	CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-22-4	Et	H	H	CH ₂ CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-22-5	Et	H	H	CH ₂ Ph	ⁱ Pr	H	F	F	OH
XXXI-22-6	Et	H	H	CH ₂ -indol-3-yl	ⁱ Pr	H	F	F	OH
XXXI-22-7	Et	H	H	CH ₂ CH ₂ SCH ₃	ⁱ Pr	H	F	F	OH
XXXI-22-8	Et	*	H	*	ⁱ Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-23.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-23-1	ⁱ Pr	H	H	H	ⁱ Pr	H	F	F	OH
XXXI-23-2	ⁱ Pr	H	H	CH ₃	ⁱ Pr	H	F	F	OH
XXXI-23-3	ⁱ Pr	H	H	CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-23-4	ⁱ Pr	H	H	CH ₂ CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-23-5	ⁱ Pr	H	H	CH ₂ Ph	ⁱ Pr	H	F	F	OH
XXXI-23-6	ⁱ Pr	H	H	CH ₂ -indol-3-yl	ⁱ Pr	H	F	F	OH
XXXI-23-7	ⁱ Pr	H	H	CH ₂ CH ₂ SCH ₃	ⁱ Pr	H	F	F	OH
XXXI-23-8	ⁱ Pr	*	H	*	ⁱ Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-24.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-24-1	^t Bu	H	H	H	ⁱ Pr	H	F	F	OH
XXXI-24-2	^t Bu	H	H	CH ₃	ⁱ Pr	H	F	F	OH
XXXI-24-3	^t Bu	H	H	CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-24-4	^t Bu	H	H	CH ₂ CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-24-5	^t Bu	H	H	CH ₂ Ph	ⁱ Pr	H	F	F	OH
XXXI-24-6	^t Bu	H	H	CH ₂ -indol-3-yl	ⁱ Pr	H	F	F	OH
XXXI-24-7	^t Bu	H	H	CH ₂ CH ₂ SCH ₃	ⁱ Pr	H	F	F	OH
XXXI-24-8	^t Bu	*	H	*	ⁱ Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-25.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-25-1	Ph	H	H	H	ⁱ Pr	H	F	F	OH
XXXI-25-2	Ph	H	H	CH ₃	ⁱ Pr	H	F	F	OH
XXXI-25-3	Ph	H	H	CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-25-4	Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-25-5	Ph	H	H	CH ₂ Ph	ⁱ Pr	H	F	F	OH
XXXI-25-6	Ph	H	H	CH ₂ -indol-3-yl	ⁱ Pr	H	F	F	OH
XXXI-25-7	Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁱ Pr	H	F	F	OH
XXXI-25-8	Ph	*	H	*	ⁱ Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-26.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-26-1	p-Me-Ph	H	H	H	ⁱ Pr	H	F	F	OH
XXXI-26-2	p-Me-Ph	H	H	CH ₃	ⁱ Pr	H	F	F	OH
XXXI-26-3	p-Me-Ph	H	H	CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-26-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁱ Pr	H	F	F	OH
XXXI-26-5	p-Me-Ph	H	H	CH ₂ Ph	ⁱ Pr	H	F	F	OH
XXXI-26-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	ⁱ Pr	H	F	F	OH
XXXI-26-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁱ Pr	H	F	F	OH
XXXI-26-8	p-Me-Ph	*	H	*	ⁱ Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-27.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-27-1	p-F-Ph	H	H	H	^t Pr	H	F	F	OH
XXXI-27-2	p-F-Ph	H	H	CH ₃	^t Pr	H	F	F	OH
XXXI-27-3	p-F-Ph	H	H	CH(CH ₃) ₂	^t Pr	H	F	F	OH
XXXI-27-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	F	F	OH
XXXI-27-5	p-F-Ph	H	H	CH ₂ Ph	^t Pr	H	F	F	OH
XXXI-27-6	p-F-Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	F	F	OH
XXXI-27-7	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	F	F	OH
XXXI-27-8	p-F-Ph	*	H	*	^t Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-28.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-28-1	p-Cl-Ph	H	H	H	^t Pr	H	F	F	OH
XXXI-28-2	p-Cl-Ph	H	H	CH ₃	^t Pr	H	F	F	OH
XXXI-28-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	^t Pr	H	F	F	OH
XXXI-28-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	F	F	OH
XXXI-28-5	p-Cl-Ph	H	H	CH ₂ Ph	^t Pr	H	F	F	OH
XXXI-28-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	F	F	OH
XXXI-28-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	F	F	OH
XXXI-28-8	p-Cl-Ph	*	H	*	^t Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-29.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-29-1	p-Br-Ph	H	H	H	^t Pr	H	F	F	OH
XXXI-29-2	p-Br-Ph	H	H	CH ₃	^t Pr	H	F	F	OH
XXXI-29-3	p-Br-Ph	H	H	CH(CH ₃) ₂	^t Pr	H	F	F	OH
XXXI-29-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	F	F	OH
XXXI-29-5	p-Br-Ph	H	H	CH ₂ Ph	^t Pr	H	F	F	OH
XXXI-29-6	p-Br-Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	F	F	OH
XXXI-29-7	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	F	F	OH
XXXI-29-8	p-Br-Ph	*	H	*	^t Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-30.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-30-1	p-I-Ph	H	H	H	^t Pr	H	F	F	OH
XXXI-30-2	p-I-Ph	H	H	CH ₃	^t Pr	H	F	F	OH
XXXI-30-3	p-I-Ph	H	H	CH(CH ₃) ₂	^t Pr	H	F	F	OH
XXXI-30-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	F	F	OH
XXXI-30-5	p-I-Ph	H	H	CH ₂ Ph	^t Pr	H	F	F	OH
XXXI-30-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	F	F	OH
XXXI-30-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	F	F	OH
XXXI-30-8	p-I-Ph	*	H	*	^t Pr	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-31.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-31-1	CH ₃	H	H	H	ⁿ Bu	H	F	F	OH
XXXI-31-2	CH ₃	H	H	CH ₃	ⁿ Bu	H	F	F	OH
XXXI-31-3	CH ₃	H	H	CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-31-4	CH ₃	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-31-5	CH ₃	H	H	CH ₂ Ph	ⁿ Bu	H	F	F	OH
XXXI-31-6	CH ₃	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	F	F	OH
XXXI-31-7	CH ₃	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	F	F	OH
XXXI-31-8	CH ₃	*	H	*	ⁿ Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-32.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-32-1	Et	H	H	H	ⁿ Bu	H	F	F	OH
XXXI-32-2	Et	H	H	CH ₃	ⁿ Bu	H	F	F	OH
XXXI-32-3	Et	H	H	CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-32-4	Et	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-32-5	Et	H	H	CH ₂ Ph	ⁿ Bu	H	F	F	OH
XXXI-32-6	Et	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	F	F	OH
XXXI-32-7	Et	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	F	F	OH
XXXI-32-8	Et	*	H	*	ⁿ Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-33.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-33-1	'Pr	H	H	H	"Bu	H	F	F	OH
XXXI-33-2	'Pr	H	H	CH ₃	"Bu	H	F	F	OH
XXXI-33-3	'Pr	H	H	CH(CH ₃) ₂	"Bu	H	F	F	OH
XXXI-33-4	'Pr	H	H	CH ₂ CH(CH ₃) ₂	"Bu	H	F	F	OH
XXXI-33-5	'Pr	H	H	CH ₂ Ph	"Bu	H	F	F	OH
XXXI-33-6	'Pr	H	H	CH ₂ -indol-3-yl	"Bu	H	F	F	OH
XXXI-33-7	'Pr	H	H	CH ₂ CH ₂ SCH ₃	"Bu	H	F	F	OH
XXXI-33-8	'Pr	*	H	*	"Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-34.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-34-1	'Bu	H	H	H	"Bu	H	F	F	OH
XXXI-34-2	'Bu	H	H	CH ₃	"Bu	H	F	F	OH
XXXI-34-3	'Bu	H	H	CH(CH ₃) ₂	"Bu	H	F	F	OH
XXXI-34-4	'Bu	H	H	CH ₂ CH(CH ₃) ₂	"Bu	H	F	F	OH
XXXI-34-5	'Bu	H	H	CH ₂ Ph	"Bu	H	F	F	OH
XXXI-34-6	'Bu	H	H	CH ₂ -indol-3-yl	"Bu	H	F	F	OH
XXXI-34-7	'Bu	H	H	CH ₂ CH ₂ SCH ₃	"Bu	H	F	F	OH
XXXI-34-8	'Bu	*	H	*	"Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-35.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-35-1	Ph	H	H	H	"Bu	H	F	F	OH
XXXI-35-2	Ph	H	H	CH ₃	"Bu	H	F	F	OH
XXXI-35-3	Ph	H	H	CH(CH ₃) ₂	"Bu	H	F	F	OH
XXXI-35-4	Ph	H	H	CH ₂ CH(CH ₃) ₂	"Bu	H	F	F	OH
XXXI-35-5	Ph	H	H	CH ₂ Ph	"Bu	H	F	F	OH
XXXI-35-6	Ph	H	H	CH ₂ -indol-3-yl	"Bu	H	F	F	OH
XXXI-35-7	Ph	H	H	CH ₂ CH ₂ SCH ₃	"Bu	H	F	F	OH
XXXI-35-8	Ph	*	H	*	"Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-36.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-36-1	p-Me-Ph	H	H	H	ⁿ Bu	H	F	F	OH
XXXI-36-2	p-Me-Ph	H	H	CH ₃	ⁿ Bu	H	F	F	OH
XXXI-36-3	p-Me-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-36-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-36-5	p-Me-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	F	F	OH
XXXI-36-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	F	F	OH
XXXI-36-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	F	F	OH
XXXI-36-8	p-Me-Ph	*	H	*	ⁿ Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-37.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-37-1	p-F-Ph	H	H	H	ⁿ Bu	H	F	F	OH
XXXI-37-2	p-F-Ph	H	H	CH ₃	ⁿ Bu	H	F	F	OH
XXXI-37-3	p-F-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-37-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-37-5	p-F-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	F	F	OH
XXXI-37-6	p-F-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	F	F	OH
XXXI-37-7	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	F	F	OH
XXXI-37-8	p-F-Ph	*	H	*	ⁿ Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-38.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-38-1	p-Cl-Ph	H	H	H	ⁿ Bu	H	F	F	OH
XXXI-38-2	p-Cl-Ph	H	H	CH ₃	ⁿ Bu	H	F	F	OH
XXXI-38-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-38-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-38-5	p-Cl-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	F	F	OH
XXXI-38-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	F	F	OH
XXXI-38-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	F	F	OH
XXXI-38-8	p-Cl-Ph	*	H	*	ⁿ Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-39.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-39-1	p-Br-Ph	H	H	H	ⁿ Bu	H	F	F	OH
XXXI-39-2	p-Br-Ph	H	H	CH ₃	ⁿ Bu	H	F	F	OH
XXXI-39-3	p-Br-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-39-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-39-5	p-Br-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	F	F	OH
XXXI-39-6	p-Br-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	F	F	OH
XXXI-39-7	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	F	F	OH
XXXI-39-8	p-Br-Ph	*	H	*	ⁿ Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-40.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-40-1	p-I-Ph	H	H	H	ⁿ Bu	H	F	F	OH
XXXI-40-2	p-I-Ph	H	H	CH ₃	ⁿ Bu	H	F	F	OH
XXXI-40-3	p-I-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-40-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	F	F	OH
XXXI-40-5	p-I-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	F	F	OH
XXXI-40-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	F	F	OH
XXXI-40-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	F	F	OH
XXXI-40-8	p-I-Ph	*	H	*	ⁿ Bu	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXI-41.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-41-1	CH ₃	H	H	H	Bz	H	F	F	OH
XXXI-41-2	CH ₃	H	H	CH ₃	Bz	H	F	F	OH
XXXI-41-3	CH ₃	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-41-4	CH ₃	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-41-5	CH ₃	H	H	CH ₂ Ph	Bz	H	F	F	OH
XXXI-41-6	CH ₃	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-41-7	CH ₃	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH
XXXI-41-8	CH ₃	*	H	*	Bz	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-42.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-42-1	Et	H	H	H	Bz	H	F	F	OH
XXXI-42-2	Et	H	H	CH ₃	Bz	H	F	F	OH
XXXI-42-3	Et	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-42-4	Et	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-42-5	Et	H	H	CH ₂ Ph	Bz	H	F	F	OH
XXXI-42-6	Et	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-42-7	Et	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH
XXXI-42-8	Et	*	H	*	Bz	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-43.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-43-1	ⁱ Pr	H	H	H	Bz	H	F	F	OH
XXXI-43-2	ⁱ Pr	H	H	CH ₃	Bz	H	F	F	OH
XXXI-43-3	ⁱ Pr	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-43-4	ⁱ Pr	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-43-5	ⁱ Pr	H	H	CH ₂ Ph	Bz	H	F	F	OH
XXXI-43-6	ⁱ Pr	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-43-7	ⁱ Pr	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH
XXXI-43-8	ⁱ Pr	*	H	*	Bz	H	F	F	OH

10 *R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-44.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-44-1	^t Bu	H	H	H	Bz	H	F	F	OH
XXXI-44-2	^t Bu	H	H	CH ₃	Bz	H	F	F	OH
XXXI-44-3	^t Bu	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-44-4	^t Bu	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-44-5	^t Bu	H	H	CH ₂ Ph	Bz	H	F	F	OH
XXXI-44-6	^t Bu	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-44-7	^t Bu	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH
XXXI-44-8	^t Bu	*	H	*	Bz	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-45.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-45-1	Ph	H	H	H	Bz	H	F	F	OH
XXXI-45-2	Ph	H	H	CH ₃	Bz	H	F	F	OH
XXXI-45-3	Ph	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-45-4	Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-45-5	Ph	H	H	CH ₂ Ph	Bz	H	F	F	OH
XXXI-45-6	Ph	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-45-7	Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH
XXXI-45-8	Ph	*	H	*	Bz	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-46.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-46-1	p-Me-Ph	H	H	H	Bz	H	F	F	OH
XXXI-46-2	p-Me-Ph	H	H	CH ₃	Bz	H	F	F	OH
XXXI-46-3	p-Me-Ph	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-46-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-46-5	p-Me-Ph	H	H	CH ₂ Ph	Bz	H	F	F	OH
XXXI-46-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-46-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH
XXXI-46-8	p-Me-Ph	*	H	*	Bz	H	F	F	OH

5 *R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-47.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-47-1	p-F-Ph	H	H	H	Bz	H	F	F	OH
XXXI-47-2	p-F-Ph	H	H	CH ₃	Bz	H	F	F	OH
XXXI-47-3	p-F-Ph	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-47-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-47-5	p-F-Ph	H	H	CH ₂ Ph	Bz	H	F	F	OH
XXXI-47-6	p-F-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-47-7	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-47-8	p-F-Ph	*	H	*	Bz	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-48.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-48-1	p-Cl-Ph	H	H	H	Bz	H	F	F	OH
XXXI-48-2	p-Cl-Ph	H	H	CH ₃	Bz	H	F	F	OH
XXXI-48-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-48-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-48-5	p-Cl-Ph	H	H	CH ₂ Ph	Bz	H	F	F	OH
XXXI-48-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-48-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH
XXXI-48-8	p-Cl-Ph	*	H	*	Bz	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-49.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-49-1	p-Br-Ph	H	H	H	Bz	H	F	F	OH
XXXI-49-2	p-Br-Ph	H	H	CH ₃	Bz	H	F	F	OH
XXXI-49-3	p-Br-Ph	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-49-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-49-5	p-Br-Ph	H	H	CH ₂ Ph	Bz	H	F	F	OH
XXXI-49-6	p-Br-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-49-7	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH
XXXI-49-8	p-Br-Ph	*	H	*	Bz	H	F	F	OH

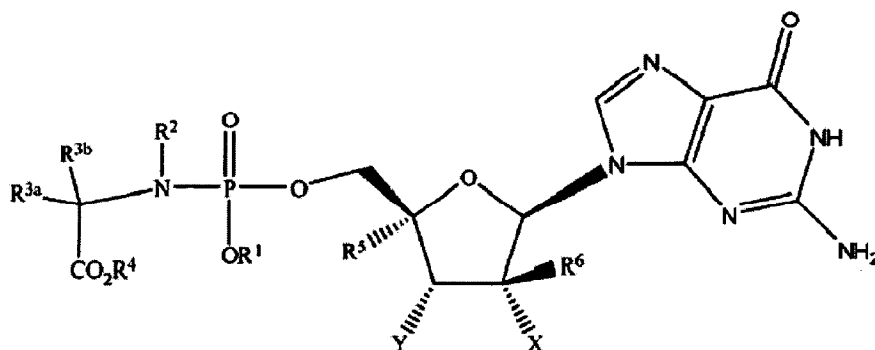
5 *R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXI-50.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-50-1	p-I-Ph	H	H	H	Bz	H	F	F	OH
XXXI-50-2	p-I-Ph	H	H	CH ₃	Bz	H	F	F	OH
XXXI-50-3	p-I-Ph	H	H	CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-50-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	F	F	OH
XXXI-50-5	p-I-Ph	H	H	CH ₂ Ph	Bz	H	F	F	OH

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXI-50-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	F	F	OH
XXXI-50-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	F	F	OH
XXXI-50-8	p-I-Ph	*	H	*	Bz	H	F	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.



XXXII

5

Table XXXII-1.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-1-1	CH ₃	H	H	H	CH ₃	H	H	F	OH
XXXII-1-2	CH ₃	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-1-3	CH ₃	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-1-4	CH ₃	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-1-5	CH ₃	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-1-6	CH ₃	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-1-7	CH ₃	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-1-8	CH ₃	*	H	*	CH ₃	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-2.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-2-1	Et	H	H	H	CH ₃	H	H	F	OH
XXXII-2-2	Et	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-2-3	Et	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-2-4	Et	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-2-5	Et	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-2-6	Et	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-2-7	Et	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-2-8	Et	*	H	*	CH ₃	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-3.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-3-1	ⁱ Pr	H	H	H	CH ₃	H	H	F	OH
XXXII-3-2	ⁱ Pr	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-3-3	ⁱ Pr	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-3-4	ⁱ Pr	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-3-5	ⁱ Pr	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-3-6	ⁱ Pr	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-3-7	ⁱ Pr	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-3-8	ⁱ Pr	*	H	*	CH ₃	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-4.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-4-1	ⁱ Bu	H	H	H	CH ₃	H	H	F	OH
XXXII-4-2	ⁱ Bu	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-4-3	ⁱ Bu	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-4-4	ⁱ Bu	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-4-5	ⁱ Bu	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-4-6	ⁱ Bu	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-4-7	ⁱ Bu	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-4-8	ⁱ Bu	*	H	*	CH ₃	H	H	F	OH

5 *R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-5.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-5-1	Ph	H	H	H	CH ₃	H	H	F	OH

N ^o	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-5-2	Ph	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-5-3	Ph	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-5-4	Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-5-5	Ph	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-5-6	Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-5-7	Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-5-8	Ph	*	H	*	CH ₃	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-6.

N ^o	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-6-1	p-Me-Ph	H	H	H	CH ₃	H	H	F	OH
XXXII-6-2	p-Me-Ph	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-6-3	p-Me-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-6-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-6-5	p-Me-Ph	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-6-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-6-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-6-8	p-Me-Ph	*	H	*	CH ₃	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-7.

N ^o	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-7-1	p-F-Ph	H	H	H	CH ₃	H	H	F	OH
XXXII-7-2	p-F-Ph	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-7-3	p-F-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-7-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-7-6	p-F-Ph	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-7-7	p-F-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-7-8	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-7-20	p-F-Ph	*	H	*	CH ₃	H	H	F	OH

5 *R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-8.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-8-1	p-Cl-Ph	H	H	H	CH ₃	H	H	F	OH
XXXII-8-2	p-Cl-Ph	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-8-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-8-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-8-5	p-Cl-Ph	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-8-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-8-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-8-8	p-Cl-Ph	*	H	*	CH ₃	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-9.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-9-1	p-Br-Ph	H	H	H	CH ₃	H	H	F	OH
XXXII-9-2	p-Br-Ph	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-9-3	p-Br-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-9-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-9-6	p-Br-Ph	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-9-7	p-Br-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-9-8	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-9-20	p-Br-Ph	*	H	*	CH ₃	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-10.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-10-1	p-I-Ph	H	H	H	CH ₃	H	H	F	OH
XXXII-10-2	p-I-Ph	H	H	CH ₃	CH ₃	H	H	F	OH
XXXII-10-3	p-I-Ph	H	H	CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-10-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	CH ₃	H	H	F	OH
XXXII-10-5	p-I-Ph	H	H	CH ₂ Ph	CH ₃	H	H	F	OH
XXXII-10-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	CH ₃	H	H	F	OH
XXXII-10-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	CH ₃	H	H	F	OH
XXXII-10-8	p-I-Ph	*	H	*	CH ₃	H	H	F	OH

5 *R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-11.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-11-1	CH ₃	H	H	H	Et	H	H	F	OH
XXXII-11-2	CH ₃	H	H	CH ₃	Et	H	H	F	OH
XXXII-11-3	CH ₃	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-11-4	CH ₃	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-11-5	CH ₃	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-11-6	CH ₃	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-11-7	CH ₃	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-11-8	CH ₃	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-12.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-12-1	Et	H	H	H	Et	H	H	F	OH
XXXII-12-2	Et	H	H	CH ₃	Et	H	H	F	OH
XXXII-12-3	Et	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-12-4	Et	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-12-5	Et	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-12-6	Et	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-12-7	Et	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-12-8	Et	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-13.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-13-1	^t Pr	H	H	H	Et	H	H	F	OH
XXXII-13-2	^t Pr	H	H	CH ₃	Et	H	H	F	OH
XXXII-13-3	^t Pr	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-13-4	^t Pr	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-13-5	^t Pr	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-13-6	^t Pr	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-13-7	^t Pr	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-13-8	^t Pr	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-14.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-14-1	'Bu	H	H	H	Et	H	H	F	OH
XXXII-14-2	'Bu	H	H	CH ₃	Et	H	H	F	OH
XXXII-14-3	'Bu	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-14-4	'Bu	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-14-5	'Bu	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-14-6	'Bu	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-14-7	'Bu	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-14-8	'Bu	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-15.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-15-1	Ph	H	H	H	Et	H	H	F	OH
XXXII-15-2	Ph	H	H	CH ₃	Et	H	H	F	OH
XXXII-15-3	Ph	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-15-4	Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-15-5	Ph	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-15-6	Ph	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-15-7	Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-15-8	Ph	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-16.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-16-1	p-Me-Ph	H	H	H	Et	H	H	F	OH
XXXII-16-2	p-Me-Ph	H	H	CH ₃	Et	H	H	F	OH
XXXII-16-3	p-Me-Ph	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-16-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-16-5	p-Me-Ph	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-16-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-16-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-16-8	p-Me-Ph	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-17.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-17-1	p-F-Ph	H	H	H	Et	H	H	F	OH
XXXII-17-2	p-F-Ph	H	H	CH ₃	Et	H	H	F	OH
XXXII-17-3	p-F-Ph	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-17-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-17-5	p-F-Ph	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-17-6	p-F-Ph	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-17-7	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-17-8	p-F-Ph	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-18.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-18-1	p-Cl-Ph	H	H	H	Et	H	H	F	OH
XXXII-18-2	p-Cl-Ph	H	H	CH ₃	Et	H	H	F	OH
XXXII-18-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-18-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-18-5	p-Cl-Ph	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-18-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-18-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-18-8	p-Cl-Ph	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-19.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-19-1	p-Br-Ph	H	H	H	Et	H	H	F	OH
XXXII-19-2	p-Br-Ph	H	H	CH ₃	Et	H	H	F	OH
XXXII-19-3	p-Br-Ph	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-19-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-19-5	p-Br-Ph	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-19-6	p-Br-Ph	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-19-7	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-19-8	p-Br-Ph	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-20.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-20-1	p-I-Ph	H	H	H	Et	H	H	F	OH
XXXII-20-2	p-I-Ph	H	H	CH ₃	Et	H	H	F	OH
XXXII-20-3	p-I-Ph	H	H	CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-20-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	Et	H	H	F	OH
XXXII-20-5	p-I-Ph	H	H	CH ₂ Ph	Et	H	H	F	OH
XXXII-20-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	Et	H	H	F	OH
XXXII-20-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	Et	H	H	F	OH
XXXII-20-8	p-I-Ph	*	H	*	Et	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-21.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-21-1	CH ₃	H	H	H	ⁱ Pr	H	H	F	OH
XXXII-21-2	CH ₃	H	H	CH ₃	ⁱ Pr	H	H	F	OH
XXXII-21-3	CH ₃	H	H	CH(CH ₃) ₂	ⁱ Pr	H	H	F	OH
XXXII-21-4	CH ₃	H	H	CH ₂ CH(CH ₃) ₂	ⁱ Pr	H	H	F	OH
XXXII-21-5	CH ₃	H	H	CH ₂ Ph	ⁱ Pr	H	H	F	OH
XXXII-21-6	CH ₃	H	H	CH ₂ -indol-3-yl	ⁱ Pr	H	H	F	OH
XXXII-21-7	CH ₃	H	H	CH ₂ CH ₂ SCH ₃	ⁱ Pr	H	H	F	OH
XXXII-21-8	CH ₃	*	H	*	ⁱ Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-22.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-22-1	Et	H	H	H	ⁱ Pr	H	H	F	OH
XXXII-22-2	Et	H	H	CH ₃	ⁱ Pr	H	H	F	OH
XXXII-22-3	Et	H	H	CH(CH ₃) ₂	ⁱ Pr	H	H	F	OH
XXXII-22-4	Et	H	H	CH ₂ CH(CH ₃) ₂	ⁱ Pr	H	H	F	OH
XXXII-22-5	Et	H	H	CH ₂ Ph	ⁱ Pr	H	H	F	OH
XXXII-22-6	Et	H	H	CH ₂ -indol-3-yl	ⁱ Pr	H	H	F	OH
XXXII-22-7	Et	H	H	CH ₂ CH ₂ SCH ₃	ⁱ Pr	H	H	F	OH
XXXII-22-8	Et	*	H	*	ⁱ Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-23.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-23-1	^t Pr	H	H	H	^t Pr	H	H	F	OH
XXXII-23-2	^t Pr	H	H	CH ₃	^t Pr	H	H	F	OH
XXXII-23-3	^t Pr	H	H	CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-23-4	^t Pr	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-23-5	^t Pr	H	H	CH ₂ Ph	^t Pr	H	H	F	OH
XXXII-23-6	^t Pr	H	H	CH ₂ -indol-3-yl	^t Pr	H	H	F	OH
XXXII-23-7	^t Pr	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	H	F	OH
XXXII-23-8	^t Pr	*	H	*	^t Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-24.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-24-1	^t Bu	H	H	H	^t Pr	H	H	F	OH
XXXII-24-2	^t Bu	H	H	CH ₃	^t Pr	H	H	F	OH
XXXII-24-3	^t Bu	H	H	CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-24-4	^t Bu	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-24-5	^t Bu	H	H	CH ₂ Ph	^t Pr	H	H	F	OH
XXXII-24-6	^t Bu	H	H	CH ₂ -indol-3-yl	^t Pr	H	H	F	OH
XXXII-24-7	^t Bu	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	H	F	OH
XXXII-24-8	^t Bu	*	H	*	^t Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-25.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-25-1	Ph	H	H	H	^t Pr	H	H	F	OH
XXXII-25-2	Ph	H	H	CH ₃	^t Pr	H	H	F	OH
XXXII-25-3	Ph	H	H	CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-25-4	Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-25-5	Ph	H	H	CH ₂ Ph	^t Pr	H	H	F	OH
XXXII-25-6	Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	H	F	OH
XXXII-25-7	Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	H	F	OH
XXXII-25-8	Ph	*	H	*	^t Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-26.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-26-1	p-Me-Ph	H	H	H	^t Pr	H	H	F	OH
XXXII-26-2	p-Me-Ph	H	H	CH ₃	^t Pr	H	H	F	OH
XXXII-26-3	p-Me-Ph	H	H	CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-26-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-26-5	p-Me-Ph	H	H	CH ₂ Ph	^t Pr	H	H	F	OH
XXXII-26-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	H	F	OH
XXXII-26-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	H	F	OH
XXXII-26-8	p-Me-Ph	*	H	*	^t Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-27.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-27-1	p-F-Ph	H	H	H	^t Pr	H	H	F	OH
XXXII-27-2	p-F-Ph	H	H	CH ₃	^t Pr	H	H	F	OH
XXXII-27-3	p-F-Ph	H	H	CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-27-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-27-5	p-F-Ph	H	H	CH ₂ Ph	^t Pr	H	H	F	OH
XXXII-27-6	p-F-Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	H	F	OH
XXXII-27-7	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	H	F	OH
XXXII-27-8	p-F-Ph	*	H	*	^t Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-28.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-28-1	p-Cl-Ph	H	H	H	^t Pr	H	H	F	OH
XXXII-28-2	p-Cl-Ph	H	H	CH ₃	^t Pr	H	H	F	OH
XXXII-28-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-28-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-28-5	p-Cl-Ph	H	H	CH ₂ Ph	^t Pr	H	H	F	OH
XXXII-28-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	H	F	OH
XXXII-28-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	H	F	OH
XXXII-28-8	p-Cl-Ph	*	H	*	^t Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-29.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-29-1	p-Br-Ph	H	H	H	^t Pr	H	H	F	OH
XXXII-29-2	p-Br-Ph	H	H	CH ₃	^t Pr	H	H	F	OH
XXXII-29-3	p-Br-Ph	H	H	CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-29-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-29-5	p-Br-Ph	H	H	CH ₂ Ph	^t Pr	H	H	F	OH
XXXII-29-6	p-Br-Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	H	F	OH
XXXII-29-7	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	H	F	OH
XXXII-29-8	p-Br-Ph	*	H	*	^t Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-30.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-30-1	p-I-Ph	H	H	H	^t Pr	H	H	F	OH
XXXII-30-2	p-I-Ph	H	H	CH ₃	^t Pr	H	H	F	OH
XXXII-30-3	p-I-Ph	H	H	CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-30-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	^t Pr	H	H	F	OH
XXXII-30-5	p-I-Ph	H	H	CH ₂ Ph	^t Pr	H	H	F	OH
XXXII-30-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	^t Pr	H	H	F	OH
XXXII-30-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	^t Pr	H	H	F	OH
XXXII-30-8	p-I-Ph	*	H	*	^t Pr	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-31.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-31-1	CH ₃	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-31-2	CH ₃	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-31-3	CH ₃	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-31-4	CH ₃	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-31-5	CH ₃	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-31-6	CH ₃	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-31-7	CH ₃	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-31-8	CH ₃	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-32.

N ^o	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-32-1	Et	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-32-2	Et	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-32-3	Et	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-32-4	Et	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-32-5	Et	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-32-6	Et	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-32-7	Et	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-32-8	Et	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-33.

N ^o	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-33-1	ⁱ Pr	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-33-2	ⁱ Pr	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-33-3	ⁱ Pr	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-33-4	ⁱ Pr	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-33-5	ⁱ Pr	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-33-6	ⁱ Pr	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-33-7	ⁱ Pr	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-33-8	ⁱ Pr	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-34.

N ^o	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-34-1	ⁱ Bu	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-34-2	ⁱ Bu	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-34-3	ⁱ Bu	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-34-4	ⁱ Bu	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-34-5	ⁱ Bu	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-34-6	ⁱ Bu	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-34-7	ⁱ Bu	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-34-8	ⁱ Bu	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-35.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-35-1	Ph	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-35-2	Ph	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-35-3	Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-35-4	Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-35-5	Ph	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-35-6	Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-35-7	Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-35-8	Ph	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-36.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-36-1	p-Me-Ph	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-36-2	p-Me-Ph	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-36-3	p-Me-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-36-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-36-5	p-Me-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-36-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-36-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-36-8	p-Me-Ph	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-37.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-37-1	p-F-Ph	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-37-2	p-F-Ph	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-37-3	p-F-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-37-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-37-5	p-F-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-37-6	p-F-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-37-7	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-37-8	p-F-Ph	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-38.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-38-1	p-Cl-Ph	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-38-2	p-Cl-Ph	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-38-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-38-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-38-5	p-Cl-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-38-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-38-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-38-8	p-Cl-Ph	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-39.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-39-1	p-Br-Ph	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-39-2	p-Br-Ph	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-39-3	p-Br-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-39-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-39-5	p-Br-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-39-6	p-Br-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-39-7	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-39-8	p-Br-Ph	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-40.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-40-1	p-I-Ph	H	H	H	ⁿ Bu	H	H	F	OH
XXXII-40-2	p-I-Ph	H	H	CH ₃	ⁿ Bu	H	H	F	OH
XXXII-40-3	p-I-Ph	H	H	CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-40-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	ⁿ Bu	H	H	F	OH
XXXII-40-5	p-I-Ph	H	H	CH ₂ Ph	ⁿ Bu	H	H	F	OH
XXXII-40-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	ⁿ Bu	H	H	F	OH
XXXII-40-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	ⁿ Bu	H	H	F	OH
XXXII-40-8	p-I-Ph	*	H	*	ⁿ Bu	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-41.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-41-1	CH ₃	H	H	H	Bz	H	H	F	OH
XXXII-41-2	CH ₃	H	H	CH ₃	Bz	H	H	F	OH
XXXII-41-3	CH ₃	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-41-4	CH ₃	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-41-5	CH ₃	H	H	CH ₂ Ph	Bz	H	H	F	OH
XXXII-41-6	CH ₃	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-41-7	CH ₃	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH
XXXII-41-8	CH ₃	*	H	*	Bz	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-42.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-42-1	Et	H	H	H	Bz	H	H	F	OH
XXXII-42-2	Et	H	H	CH ₃	Bz	H	H	F	OH
XXXII-42-3	Et	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-42-4	Et	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-42-5	Et	H	H	CH ₂ Ph	Bz	H	H	F	OH
XXXII-42-6	Et	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-42-7	Et	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH
XXXII-42-8	Et	*	H	*	Bz	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

5 Table XXXII-43.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-43-1	^t Pr	H	H	H	Bz	H	H	F	OH
XXXII-43-2	^t Pr	H	H	CH ₃	Bz	H	H	F	OH
XXXII-43-3	^t Pr	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-43-4	^t Pr	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-43-5	^t Pr	H	H	CH ₂ Ph	Bz	H	H	F	OH
XXXII-43-6	^t Pr	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-43-7	^t Pr	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH
XXXII-43-8	^t Pr	*	H	*	Bz	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-44.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-44-1	^t Bu	H	H	H	Bz	H	H	F	OH
XXXII-44-2	^t Bu	H	H	CH ₃	Bz	H	H	F	OH
XXXII-44-3	^t Bu	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-44-4	^t Bu	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-44-5	^t Bu	H	H	CH ₂ Ph	Bz	H	H	F	OH
XXXII-44-6	^t Bu	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-44-7	^t Bu	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH
XXXII-44-8	^t Bu	*	H	*	Bz	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-45.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-45-1	Ph	H	H	H	Bz	H	H	F	OH
XXXII-45-2	Ph	H	H	CH ₃	Bz	H	H	F	OH
XXXII-45-3	Ph	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-45-4	Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-45-5	Ph	H	H	CH ₂ Ph	Bz	H	H	F	OH
XXXII-45-6	Ph	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-45-7	Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH
XXXII-45-8	Ph	*	H	*	Bz	H	H	F	OH

5 *R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-46.

N ₂	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-46-1	p-Me-Ph	H	H	H	Bz	H	H	F	OH
XXXII-46-2	p-Me-Ph	H	H	CH ₃	Bz	H	H	F	OH
XXXII-46-3	p-Me-Ph	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-46-4	p-Me-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-46-5	p-Me-Ph	H	H	CH ₂ Ph	Bz	H	H	F	OH
XXXII-46-6	p-Me-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-46-7	p-Me-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-46-8	p-Me-Ph	*	H	*	Bz	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-47.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-47-1	p-F-Ph	H	H	H	Bz	H	H	F	OH
XXXII-47-2	p-F-Ph	H	H	CH ₃	Bz	H	H	F	OH
XXXII-47-3	p-F-Ph	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-47-4	p-F-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-47-5	p-F-Ph	H	H	CH ₂ Ph	Bz	H	H	F	OH
XXXII-47-6	p-F-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-47-7	p-F-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH
XXXII-47-8	p-F-Ph	*	H	*	Bz	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-48.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-48-1	p-Cl-Ph	H	H	H	Bz	H	H	F	OH
XXXII-48-2	p-Cl-Ph	H	H	CH ₃	Bz	H	H	F	OH
XXXII-48-3	p-Cl-Ph	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-48-4	p-Cl-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-48-5	p-Cl-Ph	H	H	CH ₂ Ph	Bz	H	H	F	OH
XXXII-48-6	p-Cl-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-48-7	p-Cl-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH
XXXII-48-8	p-Cl-Ph	*	H	*	Bz	H	H	F	OH

5 *R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-49.

№	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-49-1	p-Br-Ph	H	H	H	Bz	H	H	F	OH
XXXII-49-2	p-Br-Ph	H	H	CH ₃	Bz	H	H	F	OH
XXXII-49-3	p-Br-Ph	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-49-4	p-Br-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-49-5	p-Br-Ph	H	H	CH ₂ Ph	Bz	H	H	F	OH

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-49-6	p-Br-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-49-7	p-Br-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH
XXXII-49-8	p-Br-Ph	*	H	*	Bz	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

Table XXXII-50.

No	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	R ⁵	R ⁶	X	Y
XXXII-50-1	p-I-Ph	H	H	H	Bz	H	H	F	OH
XXXII-50-2	p-I-Ph	H	H	CH ₃	Bz	H	H	F	OH
XXXII-50-3	p-I-Ph	H	H	CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-50-4	p-I-Ph	H	H	CH ₂ CH(CH ₃) ₂	Bz	H	H	F	OH
XXXII-50-5	p-I-Ph	H	H	CH ₂ Ph	Bz	H	H	F	OH
XXXII-50-6	p-I-Ph	H	H	CH ₂ -indol-3-yl	Bz	H	H	F	OH
XXXII-50-7	p-I-Ph	H	H	CH ₂ CH ₂ SCH ₃	Bz	H	H	F	OH
XXXII-50-8	p-I-Ph	*	H	*	Bz	H	H	F	OH

*R² and R^{3b} joined together by (CH₂)₃ to form five-membered ring.

DOSAGE, ADMINISTRATION, AND USE

- 5 A sixth embodiment of the present invention is directed to a composition for the treatment 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, that is intended to include its salts (acid or basic addition salts), hydrates, solvates, and crystalline forms can be obtained, represented by
- 10 formula I.

It is contemplated that the formulation of the sixth embodiment can contain any of the compounds contemplated in any of the aspects of the first, second, third, fourth, and fifth embodiments or those specifically recited in the tables above or exemplified herein, either alone or in combination with another compound of the present invention.

- 15 The compounds of the present invention may be formulated in a wide variety of oral administration dosage forms and carriers. Oral administration can be in the form of tablets, coated tablets, hard and soft gelatin capsules, solutions, emulsions, syrups, or

suspensions. Compounds of the present invention are efficacious when administered by suppository administration, among other routes of administration. The most convenient manner of administration is generally oral using a convenient daily dosing regimen which can be adjusted according to the severity of the disease and the patient's response to the
5 antiviral medication.

A compound or compounds of the present invention, as well as their pharmaceutically acceptable salts, together with one or more conventional excipients, carriers, or diluents, may be placed into the form of pharmaceutical compositions and unit dosages. The pharmaceutical compositions and unit dosage forms may be comprised
10 of conventional ingredients in conventional proportions, with or without additional active compounds and the unit dosage forms may contain any suitable effective amount of the active ingredient commensurate with the intended daily dosage range to be employed. The pharmaceutical compositions may be employed as solids, such as tablets or filled capsules, semisolids, powders, sustained release formulations, or liquids such as
15 suspensions, emulsions, or filled capsules for oral use; or in the form of suppositories for rectal or vaginal administration. A typical preparation will contain from about 5% to about 95% active compound or compounds (w/w). The term "preparation" or "dosage form" is intended to include both solid and liquid formulations of the active compound and one skilled in the art will appreciate that an active ingredient can exist in different
20 preparations depending on the desired dose and pharmacokinetic parameters.

The term "excipient" as used herein refers to a compound that is used to prepare a pharmaceutical composition, and is generally safe, non-toxic and neither biologically nor otherwise undesirable, and includes excipients that are acceptable for veterinary use as well as human pharmaceutical use. The compounds of this invention can be administered
25 alone but will generally be administered in admixture with one or more suitable pharmaceutical excipients, diluents or carriers selected with regard to the intended route of administration and standard pharmaceutical practice.

A "pharmaceutically acceptable salt" form of an active ingredient may also initially confer a desirable pharmacokinetic property on the active ingredient which were

absent in the non-salt form, and may even positively affect the pharmacodynamics of the active ingredient with respect to its therapeutic activity in the body. The phrase "pharmaceutically acceptable salt" of a compound as used herein means a salt that is pharmaceutically acceptable and that possesses the desired pharmacological activity of the parent compound. Such salts include: (1) acid addition salts, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like; or formed with organic acids such as glycolic acid, pyruvic acid, lactic acid, malonic acid, malic acid, maleic acid, fumaric acid, tartaric acid, citric acid, 3-(4-hydroxybenzoyl)benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, 1,2-ethane-disulfonic acid, 2-hydroxyethanesulfonic acid, benzenesulfonic acid, 4-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, 4-toluenesulfonic acid, camphorsulfonic acid, lauryl sulfuric acid, gluconic acid, glutamic acid, salicylic acid, muconic acid, and the like or (2) basic addition salts formed with the conjugate bases of any of the inorganic acids listed above, wherein the conjugate bases comprise a cationic component selected from among Na^+ , K^+ , Mg^{2+} , Ca^{2+} , and $\text{NH}_g\text{R}^{\text{---}}_{4-g}^+$, in which $\text{R}^{\text{---}}$ is a C_{1-3} alkyl and g is a number selected from among 0, 1, 2, 3, or 4. It should be understood that all references to pharmaceutically acceptable salts include solvent addition forms (solvates) or crystal forms (polymorphs) as defined herein, of the same acid addition salt.

Solid form preparations include powders, tablets, pills, capsules, suppositories, and dispersible granules. A solid carrier may be one or more substances which may also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material. In powders, the carrier generally is a finely divided solid which is a mixture with the finely divided active component. In tablets, the active component generally is mixed with the carrier having the necessary binding capacity in suitable proportions and compacted in the shape and size desired. Suitable carriers include but are not limited to magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. Solid form preparations may contain, in addition to the active component, colorants, flavors, stabilizers, buffers, artificial and natural sweeteners, dispersants,

thickeners, solubilizing agents, and the like.

Liquid formulations also are suitable for oral administration include liquid formulation including emulsions, syrups, elixirs and aqueous suspensions. These include solid form preparations which are intended to be converted to liquid form preparations shortly before use. Emulsions may be prepared in solutions, for example, in aqueous propylene glycol solutions or may contain emulsifying agents such as lecithin, sorbitan monooleate, or acacia. Aqueous suspensions can be prepared by dispersing the finely divided active component in water with viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, and other well known suspending agents.

The compounds of the present invention may be formulated for administration as suppositories. A low melting wax, such as a mixture of fatty acid glycerides or cocoa butter is first melted and the active component is dispersed homogeneously, for example, by stirring. The molten homogeneous mixture is then poured into convenient sized molds, allowed to cool, and to solidify.

The compounds of the present invention may be formulated for vaginal administration. Pessaries, tampons, creams, gels, pastes, foams or sprays containing in addition to the active ingredient such carriers as are known in the art to be appropriate.

Suitable formulations along with pharmaceutical carriers, diluents and excipients are described in *Remington: The Science and Practice of Pharmacy 1995*, edited by E. W. Martin, Mack Publishing Company, 19th edition, Easton, Pennsylvania, which is hereby incorporated by reference. The compounds of the present invention can also be encapsulated in liposomes, such as those disclosed in U.S. Patent Nos. 6,180,134, 5,192,549, 5,376,380, 6,060,080, 6,132,763, each of which is incorporated by reference. A skilled formulation scientist may modify the formulations within the teachings of the specification to provide numerous formulations for a particular route of administration without rendering the compositions of the present invention unstable or compromising their therapeutic activity.

The modification of the present compounds to render them more soluble in water or other vehicle, for example, may be easily accomplished by minor modifications (e.g., salt formulation), which are well within the ordinary skill in the art. It is also well within the ordinary skill of the art to modify the route of administration and dosage regimen of a particular compound in order to manage the pharmacokinetics of the present compounds for maximum beneficial effect in patients.

A seventh embodiment of the present invention is directed to 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 any one of the following viral agents:

hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus and Japanese encephalitis virus.

The term "medicament" means a substance used in a method of treatment and/or prophylaxis of a subject in need thereof, wherein the substance includes, but is not limited to, a composition, a formulation, a dosage form, and the like, comprising the compound of formula I. It is contemplated that the compound of the use of the compound represented by formula I in the manufacture of a medicament for the treatment of any of the antiviral conditions disclosed herein of the seventh embodiment can be any of the compounds contemplated in any of the aspects of the first, second, third, fourth, fifth embodiments or those specifically recited in the tables above or exemplified herein, either alone or in combination with another compound of the present invention. A medicament includes, but is not limited to, any one of the compositions contemplated by the sixth embodiment of the present invention.

A eighth embodiment of the present invention is directed to a method of treatment and/or prophylaxis in a subject in need thereof said method comprises administering a therapeutically effective amount of the compound represented by formula I to the subject.

A first aspect of the eighth embodiment is directed to a method of treatment and/or prophylaxis in a subject in need thereof said method comprises administering a therapeutically effective of at least two or more different compounds falling within the scope of the compound represented by formula I to the subject.

A second aspect of the eighth embodiment is directed to a method of treatment and/or prophylaxis in a subject in need thereof said method comprises alternatively or concurrently administering a therapeutically effective of at least two compounds falling within the scope of the compound represented by formula I to the subject.

5 It is intended that a subject in need thereof is one that has any condition the result of an infection by any of the viral agents disclosed herein, which includes, but is not limited to, 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, flaviviridae viruses or pestiviruses or hepaciviruses or a viral agent causing symptoms
10 equivalent or comparable to any of the above-listed viruses.

 The term "subject" means a mammal, which includes, but is not limited to, cattle, pigs, sheep, chicken, turkey, buffalo, llama, ostrich, dogs, cats, and humans, preferably the subject is a human. It is contemplated that in the method of treating a subject thereof of the sixth embodiment can be any of the compounds contemplated in any of the aspects
15 of the first, second, and third embodiments or those specifically recited in the tables above, either alone or in combination with another compound of the present invention.

 The term "therapeutically effective amount" as used herein means an amount required to reduce symptoms of the disease in an individual. The dose will be adjusted to the individual requirements in each particular case. That dosage can vary within wide
20 limits depending upon numerous factors such as the severity of the disease to be treated, the age and general health condition of the patient, other medicaments with which the patient is being treated, the route and form of administration and the preferences and experience of the medical practitioner involved. For oral administration, a daily dosage of between about 0.1 and about 10 g, including all values in between, such as 0.25, 0.5,
25 0.75, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, and 9.5, per day should be appropriate in monotherapy and/or in combination therapy. A preferred daily dosage is between about 0.5 and about 7.5 g per day, more preferred 1.5 and about 6.0 g per day. Generally, treatment is initiated with a large initial "loading dose" to rapidly reduce or eliminate the virus following by a decreasing the dose to a level sufficient to prevent

resurgence of the infection. One of ordinary skill in treating diseases described herein will be able, without undue experimentation and in reliance on personal knowledge, experience and the disclosures of this application, to ascertain a therapeutically effective amount of the compounds of the present invention for a given disease and patient.

5 Therapeutic efficacy can be ascertained from tests of liver function including, but not limited to protein levels such as serum proteins (e.g., albumin, clotting factors, alkaline phosphatase, aminotransferases (e.g., alanine transaminase, aspartate transaminase), 5'-nucleosidase, γ -glutamyltranspeptidase, etc.), synthesis of bilirubin, synthesis of cholesterol, and synthesis of bile acids; a liver metabolic function, including,
10 but not limited to, carbohydrate metabolism, amino acid and ammonia metabolism. Alternatively the therapeutic effectiveness may be monitored by measuring HCV-RNA. The results of these tests will allow the dose to be optimized.

A third aspect of the eighth embodiment, is directed to a method of treatment and/or prophylaxis in a subject in need thereof said method comprises administering to
15 the subject a therapeutically effective of a compound represented by formula I and a therapeutically effective amount of another antiviral agent; wherein the administration is concurrent or alternative. It is understood that the time between alternative administration can range between 1-24 hours, which includes any sub-range in between including, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, and 23
20 hours. Examples of "another antiviral agents" include, but are not limited to: HCV NS3 protease inhibitors (see WO 2008010921, WO 2008010921, EP 1881001, WO 2007015824, WO 2007014925, WO 2007014926, WO 2007014921, WO 2007014920, WO 2007014922, US 2005267018, WO 2005095403, WO 2005037214, WO 2004094452, US 2003187018, WO 200364456, WO 2005028502, and WO
25 2003006490); HCV NS5B Inhibitors (see US 2007275947, US20072759300, WO2007095269, WO 2007092000, WO 2007076034, WO 200702602, US 2005-98125, WO 2006093801, US 2006166964, WO 2006065590, WO 2006065335, US 2006040927, US 2006040890, WO 2006020082, WO 2006012078, WO 2005123087, US 2005154056, US 2004229840, WO 2004065367, WO 2004003138, WO
30 2004002977, WO 2004002944, WO 2004002940, WO 2004000858, WO 2003105770,

WO 2003010141, WO 2002057425, WO 2002057287, WO 2005021568, WO
2004041201, US 20060293306, US 20060194749, US 20060241064, US 6784166, WO
2007088148, WO 2007039142, WO 2005103045, WO 2007039145, WO 2004096210,
and WO 2003037895); HCV NS4 Inhibitors (see WO 2007070556 and WO
5 2005067900); HCV NS5a Inhibitors (see US 2006276511, WO 2006120252, WO
2006120251, WO 2006100310, WO 2006035061); Toll-like receptor agonists (see WO
2007093901); and other inhibitors (see WO 2004035571, WO 2004014852, WO
2004014313, WO 2004009020, WO 2003101993, WO 2000006529).

10 A fourth aspect of the eighth embodiment, is directed to a method of treatment in
a subject in need thereof said method comprises alternatively or concurrently
administering a therapeutically effective of a compound represented by formula I and
another antiviral agent to the subject. It is understood that the time between alternative
administration can range between 1-24 hours, which includes any sub-range in between
including, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, and 23
15 hours.

A fifth aspect of the eighth embodiment, is directed to a method of treatment
and/or prophylaxis in a subject in need thereof said method comprises administering to
the subject a therapeutically effective of at least one compound represented by formula I
and a therapeutically effective amount of another antiviral agent; wherein the
20 administration is concurrent or alternative. It is understood that the time between
alternative administration can range between 1-24 hours, which includes any sub-range in
between including, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22,
and 23 hours.

25 A sixth aspect of the eighth embodiment, is directed to a method of treatment in a
subject in need thereof said method comprises alternatively or concurrently administering
a therapeutically effective of at least one compound represented by formula I and another
antiviral agent to the subject. It is understood that the time between alternative
administration can range between 1-24 hours, which includes any sub-range in between

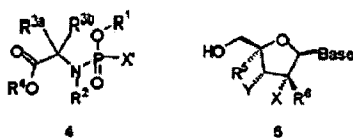
including, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, and 23 hours.

It is contemplated that the another antiviral agent includes, but is not limited to interferon - α , interferon- β , pegylated interferon- α , ribavirin, levovirin, viramidine,
5 another nucleoside HCV polymerase inhibitor, a HCV non-nucleoside polymerase inhibitor, a HCV protease inhibitor, a HCV helicase inhibitor or a HCV fusion inhibitor. When the active compound or its derivative or salt are administered in combination with another antiviral agent the activity may be increased over the parent compound. When
10 the treatment is combination therapy, such administration may be concurrent or sequential with respect to that of the nucleoside derivatives. "Concurrent administration" as used herein thus includes administration of the agents at the same time or at different times. Administration of two or more agents at the same time can be achieved by a single formulation containing two or more active ingredients or by substantially simultaneous administration of two or more dosage forms with a single active agent.

15 It will be understood that references herein to treatment extend to prophylaxis as well as to the treatment of existing conditions. Furthermore, the term "treatment" of a HCV infection, as used herein, also includes treatment or prophylaxis of a disease or a condition associated with or mediated by HCV infection, or the clinical symptoms thereof.

20 PROCESS FOR PREPARATION

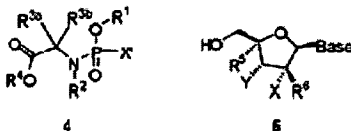
An ninth embodiment of the present invention is directed to a process for preparing the compound of formula I, which comprises reacting a suitably substituted phosphochloridate compound 4 with a nucleoside analog 5



wherein the substituents R^1 , R^2 , R^{3a} , R^{3b} , R^4 , R^5 , X , Y , R^6 , and base have their meanings as disclosed in the Detailed Description of the Invention and X' is a leaving group, such as Cl, Br, I, tosylate, mesylate, trifluoroacetate, trifluorosulfonate, pentafluorophenoxide, p-NO₂-phenoxide, or other commonly used leaving groups as disclosed in *Advanced Organic Chemistry* by March, Fourth Edition. Leaving groups and methods that can be used to effect the formation of a phosphoramidate nucleoside conjugate are found in US 20060142238 and WO 2007095269. Preferably, the leaving group is Cl.

This reaction is performed in an anhydrous aprotic solvent such tetrahydrofuran, dioxane, or both tetrahydrofuran and dioxane, or any functional equivalent thereof, with tetrahydrofuran being the preferred solvent. The reaction is typically initiated at a temperature range from -78°C to 40°C with the preferred reaction temperature being between 0°C and room temperature. The nucleoside is first stirred with a base (5 to 12 equivalents) such as N-methylimidazole, collidine, pyridine, 2,6-lutidine, 2, 6-'Bu-pyridine, etc. a tertiary amine base, such as triethylamine, diisopropylethylamine, etc., or an alkyl Grignard reagent, such as tBuMgCl, tBuMgBr, MeMgCl, MeMgBr, etc. The phosphorochloridate (3-10 equivalents) is dissolved in the reaction solvent and added to the mixture of the nucleoside and base. The reaction is then allowed to stir over a period of time at a temperature between room temperature and 40°C for a period of 30 min to 24 hr. with the preferred reaction temperature being room temperature and time being 24 hr. The solvent is removed from the reaction mixture and the product is purified by chromatography on silica gel.

A tenth embodiment of the present invention is directed to a product obtained by a process which comprises reacting a suitably substituted phosphochloridate compound 4 with a nucleoside analog 5



wherein the substituents R^1 , R^2 , R^{3a} , R^{3b} , R^4 , R^5 , X, Y, R^6 , X', and base have their meanings as disclosed in the Detailed Description of the Invention.

This reaction can be performed in an anhydrous aprotic solvent or other suitable solvent, such as tetrahydrofuran, dioxane, or a mixture of tetrahydrofuran and dioxane, with tetrahydrofuran being the preferred solvent. The reaction is typically initiated at a temperature range from -78°C to 40°C with the preferred reaction temperature being between 0°C and room temperature. The nucleoside is first stirred with a base (5 to 12 equivalents) such as N-methylimidazole, a tertiary amine base or tButyl Magnesium Chloride. A phosphorochloridate (3-10 equivalents (or suitable "phosphoro-(leaving group)-date")) is dissolved in the reaction solvent and added to the mixture of the nucleoside and base. The reaction is then allowed to stir over a period of time at a temperature between room temperature and 40°C for a period of 30 min to 24 hr. with the preferred reaction temperature being room temperature and time being 24 hr. The solvent is removed from the reaction mixture and the product is purified by chromatography on silica gel.

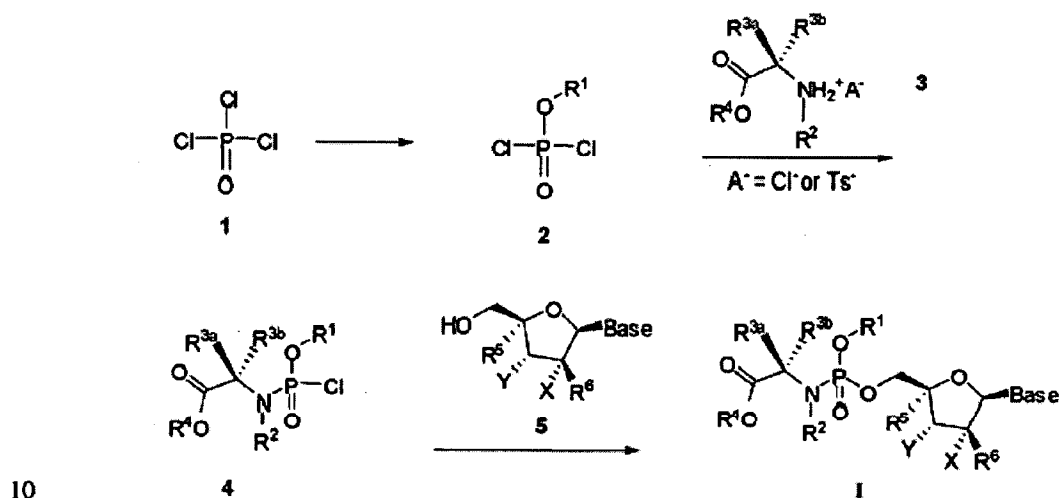
Compounds and Preparation

Phosphoramidate compounds of the present invention can be prepared by condensation of a nucleoside analog 5 with a suitably substituted phosphochloridate compound 4 (Scheme 1). The nucleoside analog is made by conventional procedures disclosed in any one of U.S. Published Application Nos. 2005/0009737, 2006/0199783, 2006/0122146, and 2007/0197463, each of which is incorporated by reference in its entirety.

Disclosed $^1\text{H-NMR}$ values were recorded on a Varian AS-400 instrument. Mass spectral data were obtain using either a Micromass-Quattromicro API or a Waters Acquity.

Thus, by way of example only, a suitably substituted phenol can be reacted with phosphorus oxychloride (1) to afford an aryloxy phosphorodichloridate 2 (see Example 1) which is subsequently treated with an acid addition salt of an α -amino acid ester in the presence of TEA to afford an aryloxy phosphorochloridate 4. This arylalkoxy-amino acid phosphoramidate is reacted with the nucleoside analog to provide the product I (for procedure see, e.g., C. McGuigan et al. Antiviral Res. 1992 17:311-321; D. Curley et al. Antiviral Res. 1990 14:345-356; McGuigan et al. Antiviral Chem. Chemother 1990 1(2):107-113).

Scheme 1



The preparation of nucleoside phosphoramidates requires reacting an appropriately substituted phosphochloridate with a nucleoside containing a free 5'-hydroxyl moiety. In cases where only one hydroxyl group is present, preparation of the phosphoramidate usually proceeds smoothly when the phosphochloridate is reacted with

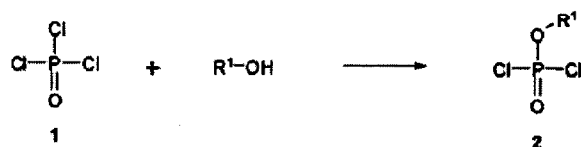
the desired nucleoside. In cases where the nucleoside contains more than one free hydroxyl group, preparation of the appropriately protected nucleoside might be required. Silyl, acetonide or other alcohol protecting groups known in the art might be warranted for protection of the sugar moiety. For protection of the nucleoside base, protecting a
5 free amino group may require amidine protection strategy.

Condensation of the phosphochloridate can be carried out on the unprotected nucleoside. Since the 5'-OH group of a nucleoside is much less hindered than the 3'-OH group, selective phosphoramidation is possible under carefully controlled conditions. After condensation to form a protected phosphoramidate nucleoside, deprotection to
10 obtain the free phosphoramidate nucleoside can be carried out using standard protocols for nucleic acid chemistry. In many cases, the desired product is readily separated from the starting material using column chromatography on silica gel. The synthetic scheme is summarized in Scheme 1.

A further understanding of the disclosed embodiments will be appreciated by
15 consideration of the following examples, which are only meant to be illustrative, and not limit the disclosed invention.

EXAMPLE 1

General Procedure for Preparation of phosphorodichloridates

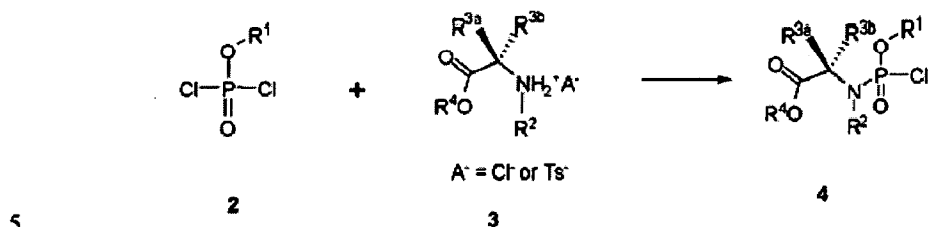


20 A solution of the appropriate phenol $\text{R}^1\text{-OH}$ (1eq) and triethylamine (1 eq.) in anhydrous ether was added dropwise to a stirred solution of phosphoryl trichloride **1** (1eq) at 0 °C over a period of 3 hours under nitrogen. Then the temperature was warmed to room temperature, and the reaction was stirred overnight. The triethylamine salt was

quickly removed with suction filtration and the filtrate concentrated *in vacuo* to dryness to afford **2** as an oil which was used without further purification.

EXAMPLE 2

General Procedure for Preparation of phosphorochloridates

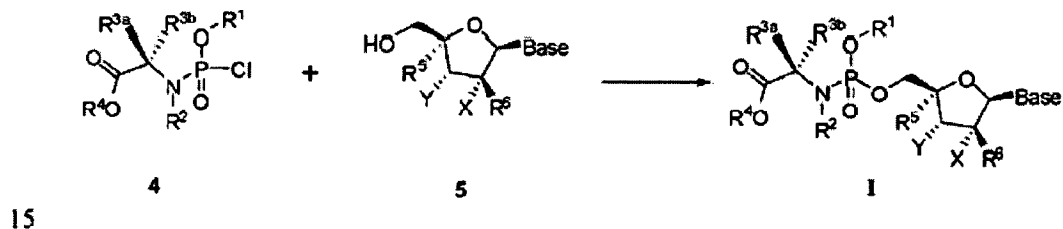


A solution of triethylamine (2eq) in anhydrous dichloromethane was added dropwise to a solution of aryloxy-phosphodichloridate **2** (1 eq) and the appropriate amino ester **3** (1 eq) in anhydrous dichloromethane with vigorous stirring at -78 °C over a period of 30 to 120 minutes. Then the reaction temperature was allowed to warm to room temperature and stirred over night. Solvent was removed. The residue was washed with ethyl ether and filtered, the filtrate was dried over reduced pressure to give **4**.

10

EXAMPLE 3

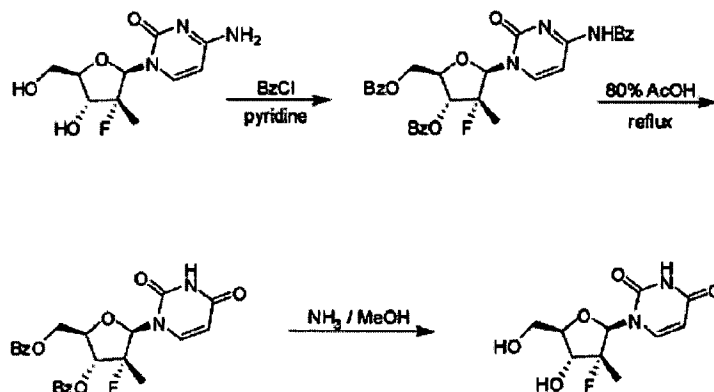
General Procedures for nucleoside phosphoramidate derivatives



A solution of the appropriate phosphorochloridate 4 (6.5 equivalents) in anhydrous tetrahydrofuran (THF) was added to a mixture of nucleoside 5 (1 equivalent) and N-methylimidazole (8 equivalents) in anhydrous THF with vigorous stirring at room temperature and the reaction mixture was stirred overnight. The solvent was removed *in vacuo* and the crude was purified by column chromatography and/or preparative thin layer chromatography to give I.

EXAMPLE 4

Preparation of 2'-deoxy-2'-fluoro-2'-C-methyluridine



2'-Deoxy-2'-fluoro-2'-C-methylcytidine (1.0g, 1 eq) (Clark, J., et al., J. Med. Chem., 2005, 48, 5504-5508) was dissolved in 10 ml of anhydrous pyridine and concentrated to dryness *in vacuo*. The resulting syrup was dissolved in 20 ml of anhydrous pyridine under nitrogen and cooled to 0°C with stirring. The brown solution was treated with benzoyl chloride (1.63g, 3eq) dropwise over 10 min. The ice bath was removed and stirring continued for 1.5h whereby thin-layer chromatography (TLC) showed no remaining starting material. The mixture was quenched by addition of water

(0.5 ml) and concentrated to dryness. The residue was dissolved in 50 mL of dichloromethane (DCM) and washed with saturated NaHCO₃ aqueous solution and H₂O. The organic phase was dried over NaSO₄ and filtered, concentrated to dryness to give N⁴,3',5'-tribenzoyl-2'-Deoxy-2'-fluoro-2'-C-methylcytidine (2.0 g, Yield: 91%).

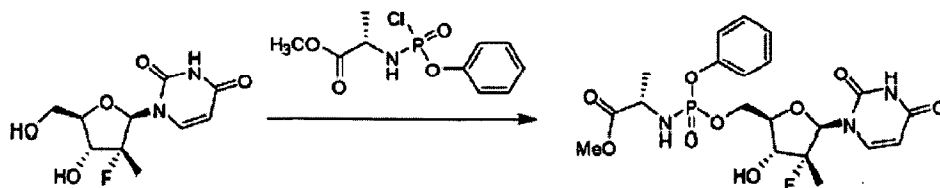
5 N⁴,3',5'-tribenzoyl-2'-Deoxy-2'-fluoro-2'-C-methylcytidine (2.0g, 1 eq) was refluxed in 80% aqueous AcOH overnight. After cooling and standing at room temperature (15 °C), most of the product precipitated and then was filtered through a sintered funnel. White precipitate was washed with water and co-evaporated with toluene to give a white solid. The filtrate was concentrated and co-evaporated with
10 toluene to give additional product which was washed with water to give a white solid. Combining the two batches of white solid gave 1.50g of 3',5'-dibenzoyl-2'-Deoxy-2'-fluoro-2'-C-methyluridine (Yield: 91%).

To a solution of 3',5'-dibenzoyl-2'-Deoxy-2'-fluoro-2'-C-methyluridine (1.5 g, 1eq) in MeOH (10 mL) was added a solution of saturated ammonia in MeOH (20mL).
15 The reaction mixture was stirred at 0 °C for 30 min, and then warmed to room temperature slowly. After the reaction mixture was stirred for another 18 hours, the reaction mixture was evaporated under reduced pressure to give the residue, which was purified by column chromatography to afford pure compound 2'-deoxy-2'-fluoro-2'-C-methyluridine (500 mg, Yield: 60 %).

20

EXAMPLE 5

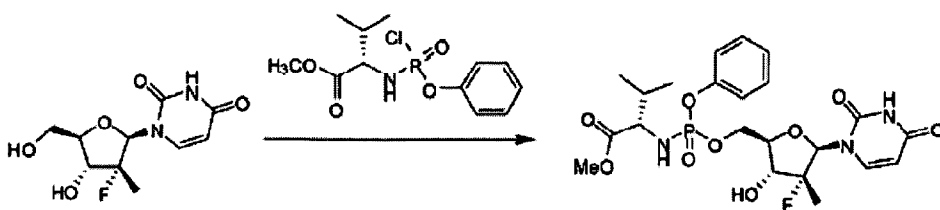
Preparation of 2'-Deoxy-2'-fluoro-2'-C-methyluridine 5'-(phenyl methoxy-alanyl phosphate)



Phenyl methoxyalaninyl phosphorochloridate (1 g, 6.5 eq) dissolved in 3 mL of THF was added to a mixture of 2'-Deoxy-2'-fluoro-2'-C-methyluridine (0.15 g, 1 eq) and N-methylimidazole (0.3 g, 8 eq) in 3 mL THF with vigorous stirring at room temperature, then the reaction was stirred overnight. Solvent was removed by reduced pressure. The resulting crude product was dissolved in methanol purified by prep-HPLC on a YMC 25x30X2 mm column using a water / acetonitrile gradient elution mobile phase. The acetonitrile and water were removed under reduced pressure to give the desired product (50.1 mg, 15.6%). ¹H NMR (DMSO-*d*₆) δ 1.20-1.27 (m, 6H), 3.58 (d, *J* = 16.0 Hz, 3H), 3.75-3.92 (m, 2H), 4.015-4.379 (m, 2H), 5.54 (t, *J* = 10.2 Hz, 1H), 5.83-5.91 (m, 1H), 6.00-6.16 (m, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.22 (s, 1H), 7.35 (t, *J* = 4.4 Hz, 2H), 7.55 (s, 1H), 11.52 (s, 1H); MS, *m/e* 502 (M+1)⁺.

EXAMPLE 6

Preparation of 2'-Deoxy-2'-fluoro-2'-C-methyluridine 5'-(phenyl methoxy-valyl phosphate)

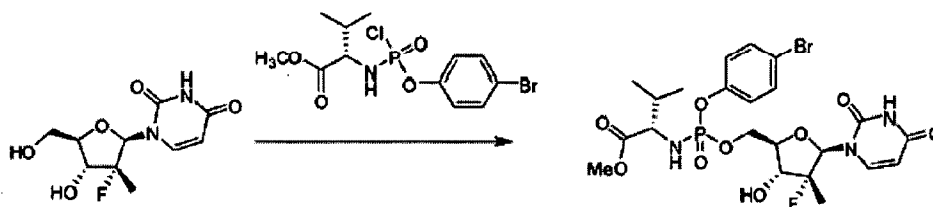


Phenyl methoxy-valyl phosphorochloridate (0.6 g, 3.6 eq) dissolved in 3 mL of THF was added to a mixture of 2'-Deoxy-2'-fluoro-2'-C-methyluridine (0.15 g, 1 eq) and N-methylimidazole (0.44 g, 9 eq) in 3 mL THF with vigorous stirring at room temperature, then the reaction was stirred overnight. Solvent was removed by reduced

pressure. The resulting crude product was dissolved in methanol purified by prep-HPLC on a YMC 25x30X2 mm column using a water / acetonitrile gradient elution mobile phase. The acetonitrile and water were removed under reduced pressure to give the desired product (60 mg, 20%). ¹H NMR (DMSO-*d*₆) δ 0.74-0.847 (m, 6H), 1.20-1.28 (m, 3H), 1.89-1.92 (m, 1H), 3.50-3.54 (m, 1H), 3.58 (d, *J* = 10.4Hz, 3H), 3.72-3.95 (m, 1H), 4.03-4.05 (m, 1H), 4.23-4.43 (m, 2H), 5.56 (t, *J* = 16.0 Hz, 1H), 5.85-5.92 (m, 1H), 6.01-6.07 (m, 1H), 7.16-7.21 (m, 3H), 7.37 (t, *J* = 8 Hz, 2H), 7.55-7.60 (m, 1H), 11.52 (s, 1H); MS, *m/e* 530 (M+1)⁺.

EXAMPLE 7

10 Preparation of 2'-Deoxy-2'-fluoro-2'-C-methyluridine 5'-(4-bromophenyl methoxy-valyl phosphate)

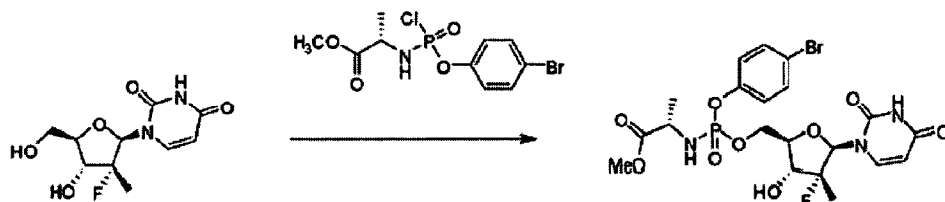


4-Bromophenyl methoxy-valyl phosphorochloridate (1 g, 3.4 eq) dissolved in 3 mL of THF was added to a mixture of 2'-deoxy-2'-fluoro-2'-C-methyluridine (0.2 g, 1 eq) and N-methylimidazole (0.35 g, 6 eq) in 3 mL THF with vigorous stirring at room temperature, then the reaction was stirred overnight. Solvent was removed by reduced pressure. The resulting crude product was dissolved in methanol purified by prep-HPLC on a YMC 25x30X2 mm column using a water / acetonitrile gradient elution mobile phase. The acetonitrile and water were removed reduced pressure to give the desired product (120 mg, 26%). ¹H NMR (DMSO-*d*₆) δ 0.72-0.82 (m, 6H), 1.19-1.26 (m, 3H),

1.86-1.92 (m, 1H), 3.48-3.50 (m, 1H), 3.56 (d, $J = 12.0$ Hz, 3H), 3.72-3.89 (m, 1H), 3.96-4.03 (m, 1H), 4.22-4.37 (m, 2H), 5.54-5.60 (m, 1H), 5.85-5.91 (m, 1H), 5.98-6.13 (m, 1H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.49-7.56 (m, 3H), 11.53 (s, 1H); MS, m/e 608 ($M+1$)⁺.

EXAMPLE 8

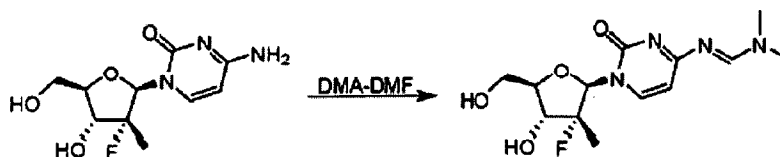
5 Preparation of 2'-Deoxy-2'-fluoro-2'-C-methyluridine 5'-(4-bromophenyl methoxy-alanyl phosphate)



4-Bromophenyl methoxy-alanyl phosphorochloridate (0.6 g, 5 eq) dissolved in 3 mL of THF was added to a mixture of 2'-deoxy-2'-fluoro-2'-C-methyluridine (0.15 g, 1 eq) and N-methylimidazole (0.3 g, 7.8 eq) in 3 mL THF with vigorous stirring at room temperature, then the reaction was stirred overnight. Solvent was removed by reduced pressure. The resulting crude product was dissolved in methanol purified by prep-HPLC on a YMC 25x30X2 mm column using a water / acetonitrile gradient elution mobile phase. The acetonitrile and water were removed under reduced pressure to give the
15 desired product (40 mg, 12 %); ¹H NMR (DMSO-*d*₆) δ 1.20-1.26 (m, 6H), 3.57 (d, $J = 2.8$ Hz, 3H), 3.84 (s, 1H), 3.97-4.03 (m, 1H), 4.21-4.25 (m, 1H), 4.33-4.37 (m, 2H), 5.54-5.60 (m, 1H), 5.83-5.89 (m, 1H), 5.98-6.19 (m, 1H), 7.16 (t, $J = 10.2$ Hz, 2H), 7.52-7.57 (m, 3H), 11.52 (s, 1 H); MS, m/e 580($M+1$)⁺.

EXAMPLE 9

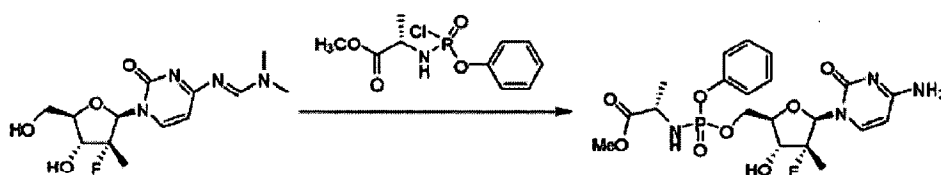
20 Preparation of N⁴-(N,N-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-C-methylecytidine



2'-Deoxy-2'-fluoro-2'-C-methylcytidine (500 mg, 1.9 mmol) was stirred with dimethylformamide dimethyl acetal in DMF (10 mL). The resulting mixture was stirred at room temperature overnight. After solvent removal the crude product was used for next step without further purification.

EXAMPLE 10

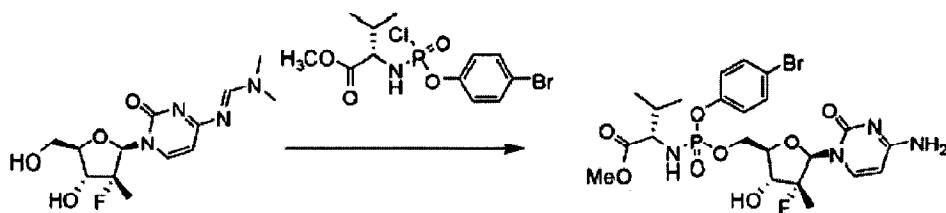
Preparation of 2'-Deoxy-2'-fluoro-2'-C-methylcytidine 5'-(phenyl methoxy-alanyl phosphate)



Phenyl methoxyalanyl phosphorochloridate (0.6 g, 6 eq) dissolved in 3 mL of THF was added to a mixture of N^4 -(*N,N*-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-C-methylcytidine (0.15 g, 1 eq) and *N*-methylimidazole (0.3 g, 7.8 eq) in 3 mL THF with vigorous stirring at room temperature, then the reaction was stirred overnight. Solvent was removed by reduced pressure. The resulting crude product was dissolved in methanol purified by prep-HPLC on a YMC 25x30X2 mm column using a water / acetonitrile gradient elution mobile phase. The acetonitrile and water were removed under reduced pressure to give the desired product (62 mg, 20.6%). ^1H NMR ($\text{DMSO}-d_6$) δ 1.16 (d, $J = 23.2$ Hz, 3H), 1.22 (d, $J = 7.2$ Hz, 3H), 3.56 (s, 3H), 3.69-3.75 (d, $J = 25.6$ Hz, 1H), 3.82-3.86 (m, 1H), 3.96-3.98 (m, 1H), 4.21-4.34 (m, 2H), 5.68 (d, $J = 7.2$ Hz, 1H), 5.75-5.77 (m, 1H), 6.07-6.16 (m, 1H), 7.15-7.19 (m, 3H), 7.2 (d, $J = 9.2$ Hz, 2H), 7.39 (t, $J = 7.8$ Hz, 2H), 7.48 (d, $J = 9.2$ Hz, 1H); MS, m/e 501($M+1$) $^+$.

EXAMPLE 11

Preparation of 2'-Deoxy-2'-fluoro-2'-C-methylcytidine 5'-(4-bromophenyl methoxy-valyl phosphate)

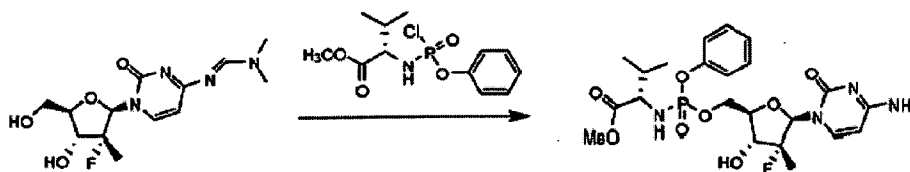


- 5 4-Bromophenyl methoxy-valyl phosphorochloridate (1.0 g, 3.4 eq.) dissolved in 3 mL of THF was added to a mixture of N⁴-(N,N-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-C-methylcytidine (0.2 g, 1 eq.) and N-methylimidazole (0.35 g, 6 eq.) in 3 mL THF with vigorous stirring at room temperature, then the reaction was stirred overnight. Solvent was removed by reduced pressure. The resulting crude product was dissolved in
- 10 methanol purified by prep-HPLC on a YMC 25x30X2 mm column using a water / acetonitrile gradient elution mobile phase. The acetonitrile and water were removed under reduced pressure to give the desired product as a white solid (59 mg, 13%); ¹H NMR (DMSO-*d*₆) δ 0.74-0.83 (m, 6H), 1.12-1.20 (m, 3H), 1.89-1.92 (m, 1H), 3.49-3.51 (m, 1H), 3.55 (s, 3H), 3.59-3.68 (m, 1H), 3.72-3.83 (m, 1H), 4.21-4.39 (m, 2H), 5.70-
- 15 5.72 (m, 1H), 5.76-5.83 (m, 1H), 6.04-6.16 (m, 1H), 7.15 (d, *J* = 13.0 Hz, 2H), 7.26 (s, 1H), 7.33 (s, 1H), 7.46-7.55 (m, 1H), 7.56 (d, *J* = 4.4 Hz, 2H) ; MS, *m/e* 607 (M+1)⁺.

EXAMPLE 12

Preparation of 2'-deoxy-2'-fluoro-2'-C-methylcytidine 5'-(phenyl methoxy-valyl phosphate)

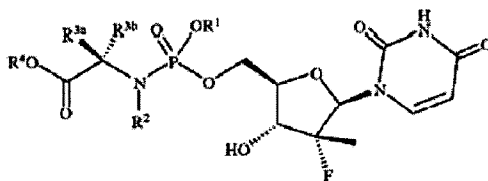
20



- Phenyl methoxy-valyl phosphorochloridate (0.6 g, 6 eq) dissolved in 3 mL of THF was added to a mixture of N^4 -(N,N -dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-C-methylcytidine (0.15 g, 1 eq) and N -methylimidazole (0.3 g, 7.8 eq) in 3 mL THF with vigorous stirring at room temperature, then the reaction was stirred overnight. Solvent was removed by reduced pressure. The resulting crude product was dissolved in methanol purified by prep-HPLC on a YMC 25x30X2 mm column using a water / acetonitrile gradient elution mobile phase. The acetonitrile and water were removed under reduced pressure to give the desired product as a white solid (86 mg, 42.9 %). ^1H NMR (DMSO- d_6) δ 0.72-0.80 (m, 6H), 1.09-1.18 (m, 3H), 1.87-1.92 (m, 1H), 3.47-3.51 (m, 1H), 3.58 (s, 3H), 3.71-3.75 (m, 1H), 3.97 (t, J = 11.2 Hz, 1H), 4.22-4.37 (m, 2H), 5.70 (d, J = 8.0 Hz, 1H), 5.76-5.84 (m, 1H), 6.01-6.15 (m, 1H), 7.13-7.18 (m, 3H), 7.27 (s, 2H), 7.34 (d, J = 4.0 Hz, 2H), 7.46-7.50 (m, 1H); MS, m/e 529 ($M+1$) $^+$.

EXAMPLES

- Example numbers 13-54 and 56-66 are prepared using similar procedures described for examples 5-8. The example number, compound identification, and NMR/MS details are shown below:



Ex.	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	NMR/MS
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Ex.	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	NMR/MS
13	Ph	H	H	Me	Et	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.12-1.16 (m, 3H), 1.20-1.28(m,6H), 3.70-3.90 (m, 2H), 4.00-4.08 (m, 3H), 4.18-4.45 (m, 2H), 5.52-5.58 (m, 1H), 5.85-5.98 (m, 1H), 6.00-6.20 (m, 2H), 7.16-7.23 (m, 3H), 7.37-7.40 (m, 2H), 7.54-7.60 (m, 1H), 11.54 (s,1H); MS, m/e 516.1 (M+1) ⁺
14	1-Naph	H	H	Me	Bn	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.18-1.30 (m, 6H), 3.78-4.10 (m, 3H), 4.38-4.49 (m, 2H), 4.99-5.11 (m, 2H), 5.28-5.40 (m, 1H), 5.85-6.10 (m, 2H), 6.30-6.41 (m, 1H), 7.28-7.32 (m, 5H), 7.41-7.60 (m, 5H), 7.73-7.76(m, 1H) , 7.94-8.11(m, 1H) , 8.13-8.15(m, 1H) , 11.50 (s,1H) ; MS, m/e 628.4 (M+1) ⁺
15	Ph	H	H	H	Me	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.22 (d, J=22.4 Hz, 3H), 3.59(s, 3H), 3.63-3.69 (m, 2H), 3.74-3.8(m, 1H), 4.02(d, J=11.2 Hz, 1H), 4.23-4.28(m, 1H), 4.40-4.43 (m, 1H), 5.57-5.60 (m, 1H), 5.89(d, J=6.8 Hz, 1H), 6.00-6.06(m, 2H), 7.15-7.23 (m, 3H), 7.35-7.39 (m, 2H),7.52(d, J=8 Hz, 1H), 11.52(s, 1H) ; MS, m/e 487.97 (M+1) ⁺
16	2,4-Cl-Ph	H	H	Me	Me	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.22-1.28 (m, 6H), 3.57-3.60 (m, 3H), 3.84-3.92 (m, 2H), 4.00-4.04 (m, 1H), 4.31-4.44 (m, 2H), 5.54-5.61 (m, 1H), 5.85-6.10 (m, 2H), 6.32-6.43 (m, 1H), 7.44-7.54 (m, 3H), 7.72-7.75 (m, 1H), 11.54 (s,1H) ; MS, m/e 570.2 (M+1) ⁺
17	1-Naph	H	H	Me	Me	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.15-1.27 (m, 6H), 3.51-3.55 (d, 3H), 3.85-3.96 (m, 2H), 4.00-4.10(m, 1H), 4.30-4.46 (m, 2H), 5.31-5.39 (m, 1H), 5.89-6.05 (m, 2H), 6.22-6.34 (m, 1H), 7.44-7.60 (m, 5H), 7.73-7.77 (m, 1H), 7.93-7.96 (m, 1H), 8.12-8.14 (m, 1H),11.50(s,1H) ; MS, m/e 552.1 (M+1) ⁺
18	Ph	*	H	*	Me	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.19 (d, J=22.8 Hz, 3H), 1.69-1.84 (m, 3H), 1.99-2.04 (m, 1H), 3.16-3.21 (m, 2H), 3.58 (s, 3H), 3.68-3.8 (m, 1H), 4.00 (m, 1H), 4.01-4.13 (m, 1H), 4.22-4.25 (m, 1 H), 4.5 (d, J = 11.2 Hz, 1H), 5.54 (d, J = 8.0 Hz, 1H), 5.86 (s, 1H), 5.6 (d, J = 19.6 Hz, 1H), 7.15-7.2 (m, 3H), 7.34 (t, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 1H), 11.38 (s, 1H) ; MS, m/e 527.93(M+1) ⁺
19	Ph	H	H	Me	n-Bu	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.80-0.90 (m, 3H), 1.20-1.35 (m, 8H), 1.48-1.55 (m, 2H), 3.78-3.88 (m, 2H), 3.95-4.08 (m, 3H), 4.22-4.45 (m, 2H), 5.55-5.57(t, 1H), 5.85-6.18 (m, 3H), 7.14-7.23 (m, 3H), 7.35-7.40 (m, 2H), 7.51-7.60 (d, 1H), 11.50 (s,1H) ; MS, m/e 544.2 (M+1) ⁺
20	Ph	H	H	Me	Bn	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.20-1.30 (m, 6H), 3.72-4.05 (m, 3H), 4.23-4.27 (m, 1H), 4.32-4.45 (m, 1H), 5.07-5.10(t, 2H), 5.52-5.56(t , 1H), 5.86-6.10 (m, 2H), 6.13-6.21(m,1H), 7.15-7.21 (m, 3H), 7.29-7.40 (m, 7H), 7.51-7.56 (d, 1H), 11.50 (s,1H) ; MS, m/e 578.2 (M+1) ⁺
21	4-F-Ph	H	H	Me	Me	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.28-1.34 (m, 6H), 3.65(d, J= 4 Hz, 3H), 3.85-3.96 (m, 2H), 4.06-4.12 (m, 1H), 4.30-4.34 (m,1H), 4.40-4.47 (m, 1H), 5.62-5.67 (m, 1H), 5.94-6.01(m, 1H), 6.09 (d, J=18.8 Hz, 1H), 6.17-6.26 (m, 1H), 7.27-7.33(m, 4H), 7.62 (d, J = 7.6 Hz, 1H), 11.61 (s, 1H) ; MS, m/e 519.94(M+1) ⁺
22	4-Cl-Ph	H	H	Me	Me	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.22-1.28 (m, 6H), 3.58 (d, 2H), 3.70-3.95(m,2H), 3.95-4.08 (m,1H), 4.23-4.45 (m, 2H), 5.55-5.61(t , 1H),

Ex.	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	NMR/MS
						5.85-6.10 (m, 2H), 6.15-6.23(m,1H), 7.20-7.26 (m, 2H), 7.43-7.46 (m, 2H), 7.54-7.57 (d, 1H), 11.50 (s, 1H); MS, m/e 536.1 (M+1)+
23	3,4-Cl-Ph	H	H	Me	Me	1H NMR (DMSO-d ₆) δ 1.13 (m, 6H), 3.49 (s, 3H), 3.61-3.85 (m, 2H), 3.90-3.93 (m, 1H), 4.16-4.22 (m, 1H), 4.27-4.31 (m, 1H), 5.47-5.52 (m, 1H), 5.82 (d, J = 11.6 Hz, 1H), 5.93(d, J = 19.2 Hz, 1H), 6.15-6.25 (m, 1H), 7.13 (t, J = 9.6 Hz, 1H), 7.43 (d, J = 12Hz, 2H), 7.57 (d, J = 6.0 Hz, 1H), 11.43(s, 1H); MS, m/e 569.85 (M+1)+
24	Ph	H	H	Me	2-Bu	1H NMR (DMSO-d ₆) δ 0.83 (d, J = 6.8 Hz, 6H), 1.20-1.26 (m, 6H), 1.79-1.86 (m, 1H), 3.73-3.90 (m, 4H), 4.01 (t, J = 11.2 Hz, 1H), 4.21-4.28 (m, 1H), 4.33-4.42 (m, 1H), 5.54 (t, J = 7.6 Hz, 1H), 5.85-5.92 (m, 1H), 5.99-6.13 (m, 2H), 7.19 (t, J = 8 Hz, 3H), 7.36 (t, J = 7.6 Hz, 2H), 7.53 (d, J = 7.6 Hz, 1H), 11.52 (s, 1H); MS, m/e 544.00 (M+1)+
25	Ph	H	H	Me	i-Pr	1H NMR (DMSO-d ₆) δ 1.13-1.28 (m, 12H), 3.74-3.81 (m, 2H), 3.95-4.08 (m, 1H), 4.20-4.45 (m, 2H), 4.83-4.87 (m, 1H), 5.52-5.58 (m, 1H), 5.84-6.15 (m, 3H), 7.17-7.23 (m, 3H), 7.35-7.39 (m, 2H), 7.54-7.57 (m, 1H), 11.50 (s, 1H); MS, m/e 530.2 (M+1)+
26	4-MeO-Ph	H	H	Me	n-Bu	1HNMR (400MHz, DMSO-d ₆): δ =0.78-0.82 (m, 3H), 1.29-1.47 (m, 8H), 1.49-1.54 (m, 2H), 3.66-3.87 (m, 5H), 3.96-4.02 (m, 3H), 4.21-4.39 (m, 2H), 5.57 (t, J = 12.0Hz, 1H), 5.84-6.05 (m, 3H), 6.90 (dd, J1 = 8.0Hz, J2 = 4.0Hz, 2H), 7.09-7.14 (dd, J1 = 16.0Hz, J2 = 4.0Hz, 2H), 7.55 (d, J = 8.0Hz, 1H), 11.48-11.62 (s, 1H)
27	4-F-Ph	H	H	Me	Et	1H NMR (DMSO-d ₆) δ 1.12-1.28 (m, 9H), 3.72-3.94(m,2H), 3.98-4.10 (m,3H), 4.21-4.42(m,2H), 5.55-5.61 (t, 1H), 5.85-6.20 (m, 3H), 7.18-7.25 (m,4H), 7.55-7.58 (d, 1H), 11.50 (s,1H); MS, m/e 533.90 (M+1)+
28	4-F-Ph	H	H	Me	i-Pr	1H NMR (DMSO-d ₆) δ 1.13-1.30 (m, 12H), 3.74-3.85(m,2H), 3.98-4.06 (m,1H), 4.23-4.41(m,2H), 4.83-4.87 (m, 1H), 5.55-5.61 (t, 1H), 5.85-6.12 (m, 3H), 7.18-7.24 (m,4H), 7.55-7.58 (d, 1H), 11.50 (s,1H); MS, m/e 547.91 (M+1)+
29	4-F-Ph	H	H	Me	Bn	1H NMR (DMSO-d ₆) δ 1.10-1.23 (m, 6H), 3.65-3.89(m,3H), 4.10-4.30 (m,2H), 4.96-5.00(m,2H), 5.46-5.50 (t, 1H), 5.75-5.96 (m, 2H), 6.04-6.12(m,1H), 7.05-7.11 (m,4H), 7.20-7.24 (d, 5H), 7.42-7.45(d,1H), 11.50 (s,1H); MS, m/e 595.94 (M+1)+
30	4-MeO-Ph	H	H	Me	i-Pr	1HNMR (400MHz, DMSO-d ₆): δ =1.15-1.27 (m, 12H), 3.71-3.89 (m, 5H), 3.98-4.02 (m, 1H), 4.22-4.25 (m, 1H), 4.33-4.39 (m, 1H), 4.84-4.87 (m, 1H), 5.57 (t, J = 12.0Hz, 1H), 5.91-6.03 (m, 3H), 6.90 (d, J = 8.0Hz, 2H), 7.09-7.14 (m, 2H), 7.55 (d, J = 8.0Hz, 1H), 11.51 (s, 1H)
31	2-Cl-Ph	H	H	Me	Bn	1H NMR (DMSO-d ₆) δ 1.23 (m, 6 H), 3.93-4.00 (m, 3 H), 4.27-4.40 (m, 2H), 5.0(t, J = 7.2 Hz, 2 H), 5.53 (m, 1 H), 5.80-6.0(m, 2 H), 6.30(m, 1H), 7.15 (d, J = 2.4 Hz, 1 H), 7.27 (m, 6 H), 7.51 (m, 3 H), 11.5 (s, 1 H); MS, m/e 579.87(M+1)+ / 596.78 (M+18)+
32	2,4-Cl-Ph	H	H	Me	n-Bu	1H NMR (DMSO-d ₆) δ =0.82 (m, 3 H), 1.23 (m, 8 H), 1.47 (m, 2 H), 3.86 (m, 2 H), 3.84 (m, 3 H), 4.27-4.43 (m, 2H), 5.5 (m, 1 H), 6.02 (m, 2 H), 6.35(m, 1H), 7.44 (m, 3 H), 7.77 (m, 1 H), 11.5 (s, 1 H); MS, m/e 611.87(M+1)+
33	4-Me-Ph	H	H	Me	i-Pr	1H NMR (DMSO-d ₆) δ 1.14-1.27 (m, 12H), 2.17-2.26 (m, 3H), 3.73-3.82 (m, 1H), 3.99-4.02 (m, 1H), 4.23-4.26 (m, 1H), 4.37-4.40 (m,

Ex.	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	NMR/MS
						¹ H, 4.82-4.88 (m, 1H), 5.52-5.58 (m, 1H), 5.85-6.07 (m, 3H), 7.01-7.20 (m, 4H), 7.55 (d, J = 16Hz, 1H), 11.51 (s, 1H); MS, m/e 543.98 (M+1) ⁺ ; 1108.86 (2M+23) ⁺
34	4-F-Ph	H	H	Me	n-Bu	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.82-0.89 (m, 3H), 1.20-1.31 (m, 8H), 1.48-1.53 (m, 2H), 3.77-3.90 (m, 2H), 3.95-4.10 (m, 3H), 4.21-4.45 (m, 2H), 5.56-5.61 (t, 1H), 5.83-6.20 (m, 3H), 7.18-7.25 (m, 4H), 7.55-7.58 (d, 1H), 11.50 (s, 1H); MS, m/e 584.1 (M+23) ⁺
35	3,4-diCl-Ph	H	H	Me	Et	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.12-1.31 (m, 9H), 3.77-3.92 (m, 2H), 3.95-4.08 (m, 3H), 4.21-4.45 (m, 2H), 5.56-5.62 (t, 1H), 5.80-6.11 (m, 2H), 6.18-6.33 (m, 1H), 7.18-7.25 (m, 1H), 7.49-7.56 (d, 2H), 7.62-7.67 (m, 1H), 11.50 (s, 1H); MS, m/e 606.1 (M+23) ⁺
36	2-Cl-Ph	H	H	Me	i-Pr	¹ H NMR (400MHz, DMSO- <i>d</i> ₆) δ 1.12-1.16 (m, 6H), 1.21-1.27 (m, 6H), 3.79-3.85 (m, 2H), 4.00-4.07 (m, 1H), 4.28-4.32 (m, 1H), 4.38-4.43 (m, 1H), 4.83-4.87 (m, 1H), 5.56 (dd, J1=16.0Hz, J2=8.0Hz, 1H), 5.85-6.12 (m, 2H), 6.20-6.33 (m, 1H), 7.19-7.22 (m, 1H), 7.33 (t, J=16.0Hz, 1H), 7.48-7.55 (m, 3H), 11.55 (s, 1H)
37	4-MeO-Ph	H	H	Me	Bn	¹ H NMR (400MHz, DMSO- <i>d</i> ₆) δ 1.19-1.26 (m, 6H), 3.69-3.70 (s, 3H), 3.87 (m, 2H), 3.99 (m, 1H), 4.20-4.21 (m, 1H), 4.35 (m, 1H), 5.07-5.09 (m, 2H), 5.54 (t, J = 16.0Hz, 1H), 5.85-5.92 (m, 1H), 6.04-6.10 (m, 2H), 6.86 (d, J = 8.0Hz, 2H), 7.09 (dd, J1=16.0Hz, J2=4.0Hz, 2H), 7.30-7.34 (m, 5H), 7.53 (s, 1H), 11.52 (s, 1H)
38	Ph	H	H	Me	n-Pen	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.79-0.81 (m, 3H), 1.17-1.23 (m, 10H), 3.74-3.81 (m, 2H), 3.94-3.96 (m, 3H), 4.19-4.36 (m, 2H), 5.49-5.54 (m, 1H), 5.87-6.08 (m, 3H), 7.14-7.33 (m, 3H), 7.31-7.35 (m, 2H), 7.51 (d, J = 8Hz, 1H), 11.51 (s, 1H); MS, m/e 557.9 (M+1) ⁺ ; 1136.88 (2M+23) ⁺
39	4-Cl-Ph	H	H	Me	i-Pr	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.04-1.19 (m, 12H), 3.76-3.80 (m, 2H), 3.98-4.08 (m, 1H), 4.42-4.42 (m, 2H), 4.82-4.85 (m, 1H), 5.55-5.60 (m, 1H), 5.80-6.20 (m, 3H), 7.20-7.2 (m, 2H), 7.43 (d, J = 8.8Hz, 1H), 7.54 (d, J = 8Hz, 1H), 11.51 (s, 1H); MS, m/e 563.88 (M+1) ⁺ ; 1148.73 (2M+23) ⁺
40	4-Cl-Ph	H	H	Me	n-Bu	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.85 (t, J = 7.2 Hz, 3H), 1.22-1.33 (m, 8H), 1.45-1.53 (m, 2H), 3.80-3.87 (m, 2H), 3.96-4.04 (m, 3H), 4.24-4.27 (m, 1H), 4.35-4.39 (m, 1H), 5.56-5.61 (m, 1H), 5.82-6.11 (m, 2H), 6.15-6.18 (m, 1H), 7.20-7.56 (m, 4H), 7.51-7.57 (m, 1H), 11.54 (s, 1H); MS, m/e 577.95 (M+1) ⁺
41	4-Cl-Ph	H	H	Me	Et	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.14 (t, J = 7.0Hz, 3H), 1.20-1.28 (m, 6H), 3.77-3.88 (m, 2H), 3.99-4.07 (m, 3H), 4.24-4.28 (m, 1H), 4.34-4.43 (m, 1H), 5.56-5.61 (m, 1H), 5.86-6.13 (m, 2H), 6.15-6.24 (m, 1H), 7.20-7.26 (m, 2H), 7.44 (d, J = 7.6Hz, 2H), 7.55 (d, J = 7.6Hz, 1H), 11.55 (s, 1H); MS, m/e 549.11 (M+1) ⁺
42	4-Me-Ph	H	H	Me	n-Bu	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.79-0.83 (m, 3H), 1.17-1.28 (m, 8H), 1.45-1.47 (m, 2H), 2.22 (d, J = 2.8Hz, 1H), 3.70-3.90 (m, 2H), 3.95-3.98 (m, 3H), 4.10-4.40 (m, 2H), 5.51 (t, 1H), 5.80-5.90 (m, 1H), 5.95-6.05 (m, 2H), 7.02-7.06 (m, 2H), 7.51 (t, J = 4.2Hz, 4H), 7.51 (d, 1H), 11.51 (s, 1H); MS, m/e 557.99 (M+1) ⁺ ; 1136.84 (2M+23) ⁺

Ex.	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	NMR/MS
43	4-Mc-Phc	H	H	Me	Bn	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.16-1.24 (m, 6H), 2.22 (s, 3H), 3.63-4.03 (m, 3H), 4.11-4.38 (m, 2H), 5.04-5.05 (m, 2H), 5.48-5.50 (m, 1H), 5.77-5.87 (m, 1H), 5.90-6.11 (m, 2H), 6.98-7.10 (m, 4H), 7.28-7.32 (m, 5H), 7.50 (t, 1H), 11.48 (s, 1H); MS, <i>m/e</i> 592.00 (M+1) ⁺ .
44	Ph	H	H	Et	Me	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.70-0.80 (m, 3H), 1.11-1.26 (m, 3H), 1.42-1.61 (m, 2H), 3.50-3.54 (m, 3H), 3.58-3.80 (m, 2H), 3.91-4.02 (m, 1H), 4.12-4.38 (m, 2H), 5.47-5.52 (m, 1H), 5.90-6.03 (m, 2H), 7.08-7.16 (m, 3H), 7.26-7.35 (m, 2H), 7.48 (t, 1H), 11.45 (s, 1H); MS, <i>m/e</i> 515.95 (M+1) ⁺ ; 1052.82 (2M+23) ⁺ .
45	Ph	H	H	Me	4-F-Bn	¹ H NMR (400MHz, DMSO- <i>d</i> ₆) δ 1.20-1.26 (m, 6H), 3.80-3.93 (m, 2H), 3.98 (s, 1H), 4.25-4.26 (m, 1H), 4.36-4.37 (m, 1H), 5.07 (s, 2H), 5.52-5.55 (m, 1H), 5.86-5.87 (m, 1H), 5.98-6.04 (m, 1H), 6.14-6.17 (m, 1H), 7.15-7.20 (m, 5H), 7.36 (dd, <i>J</i> = 20.0, 8.0 Hz, 4H), 7.54 (s, 1H), 11.55 (s, 1H).
46	4-Cl-Ph	H	H	Me	n-Bu	¹ H NMR (400MHz, DMSO- <i>d</i> ₆) δ 1.21-1.28 (m, 6H), 3.71-3.88 (m, 1H), 3.91-3.98 (m, 1H), 4.00-4.01 (m, 1H), 4.23-4.27 (m, 1H), 4.35-4.38 (m, 1H), 5.08 (d, <i>J</i> = 4.0 Hz, 2H), 5.57 (dd, <i>J</i> = 12.0, 8.0 Hz, 1H), 5.91 (d, <i>J</i> = 8.0 Hz, 1H), 6.01 (d, <i>J</i> = 8.0 Hz, 1H), 6.22-6.24 (m, 1H), 7.17-7.23 (m, 2H), 7.31-7.40 (m, 7H), 7.53 (s, 1H), 11.50 (s, 1H).
47	Ph	H	H	Me	3-Me-1-Bu	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.80-0.82 (m, 6H), 1.18-1.40 (m, 8H), 1.50-1.58 (m, 1H), 3.71-3.82 (m, 3H), 3.97-3.4.01 (m, 3H), 4.21-4.40 (m, 2H), 5.30 (t, <i>J</i> = 8.6 Hz, 1H), 5.81-6.10 (m, 3H), 7.15-7.20 (m, 3H), 7.32-7.36 (m, 2H), 7.48 (d, <i>J</i> = 8.4 Hz, 1H), 11.38 (s, 1H); MS, <i>m/e</i> 557.98 (M+1) ⁺ ; 1136.88 (2M+23) ⁺ .
48	3,4-diCl-Ph	H	H	Me	Bn	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.05-1.37 (m, 6H), 3.71-3.82 (m, 1H), 3.87-4.02 (m, 2H), 4.28-4.29 (m, 1H), 4.36-4.38 (m, 1H), 5.04 (d, <i>J</i> = 5.2 Hz, 2H), 5.55-5.64 (m, 1H), 5.85-5.94 (m, 1H), 6.00-6.05 (m, 1H), 6.29-6.40 (m, 1H), 7.17-7.24 (m, 1H), 7.30-7.41 (m, 5H), 7.45-7.58 (m, 2H), 7.61 (d, <i>J</i> = 4.0 Hz, 1H), 11.53 (s, 1H); MS, <i>m/e</i> 545.80 (M+1) ⁺ .
49	Ph	H	H	Me	c-Hex	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.18-1.41 (m, 12H), 1.59-1.67 (m, 4H), 3.74-13.80 (m, 1H), 3.96-4.02 (m, 1H), 4.19-4.26 (m, 1H), 4.31-4.39 (m, 1H), 4.60 (s, 1H), 5.52 (t, <i>J</i> = 7.8 Hz, 1H), 5.80-6.07 (m, 3H), 7.15-7.20 (m, 3H), 7.32-7.36 (m, 2H), 7.52 (d, <i>J</i> = 8 Hz, 1H), 11.50 (s, 1H); MS, <i>m/e</i> 569.98 (M+1) ⁺ ; 592.14 (M+23) ⁺ .
50	Ph	H	Me	H	n-Bu	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.76 (t, <i>J</i> = 7.2 Hz, 3H), 1.10-1.22 (m, 8H), 1.38-1.43 (m, 2H), 3.72-3.75 (m, 2H), 3.87-3.93 (m, 3H), 4.14-4.21 (m, 1H), 4.23-4.33 (m, 1H), 5.46-5.54 (m, 1H), 5.84-6.11 (m, 3H), 7.09-7.14 (m, 2H), 7.27-7.32 (m, 2H), 7.34-7.51 (m, 1H), 11.47 (s, 1H); MS, <i>m/e</i> 543.98 (M+1) ⁺ .
51	Ph	H	Me	H	i-Pr	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.39 (d, <i>J</i> = 7.2 Hz, 6H), 1.19-1.29 (m, 6H), 3.65-3.75 (m, 2H), 3.95-4.05 (m, 1H), 4.20-4.22 (m, 1H), 4.31-4.33 (m, 1H), 4.79-4.82 (m, 1H), 5.48-5.57 (m, 1H), 5.84-5.91 (m, 1H), 5.96-6.07 (m, 2H), 7.12-7.35 (m, 5H), 7.44-7.54 (m, 1H), 11.49 (s, 1H); MS, <i>m/e</i> 529.96 (M+1) ⁺ .
52	Ph	H	Me	H	Bn	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.18-1.28 (m, 6H), 3.70-3.83 (m, 1H), 3.87-3.94 (m, 1H), 3.99-4.01 (m, 1H), 4.23-4.26 (m, 1H), 4.33-4.37 (m,

Ex.	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	NMR/MS
53	2-Cl-Ph	H	H	Mc	n-Bu	¹ H), 5.03-5.12 (m, 2H), 5.51-5.59 (m, 1H), 5.87-5.90 (m, 1H), 5.95-6.07 (m, 1H), 6.10-6.27 (m, 1H), 7.15-7.23 (m, 3H), 7.31-7.38 (m, 7H), 7.47-7.56 (m, 1H), 11.50 (s, 1H); MS, m/e 577.99 (M+1) ⁺ ¹ H NMR (400MHz, DMSO-d ₆): δ 0.81-0.86 (m, 3H), 1.21-1.31 (m, 8H), 1.46-1.52 (m, 2H), 3.84-3.90 (m, 2H), 3.97-4.04 (m, 3H), 4.27-4.41 (m, 2H), 5.53-5.58 (m, 1H), 5.82-5.95 (m, 1H), 5.96-6.10 (m, 1H), 6.27-6.31 (m, 1H), 7.19-7.22 (m, 1H), 7.34 (dd, J = 8.0, 4.0 Hz, 1H), 7.47-7.55 (m, 3H), 11.55 (s, 1H)
54	4-Br-Ph	H	H	Mc	i-Pr	¹ H NMR (400MHz, DMSO-d ₆): δ 1.10-1.14 (m, 6H), 1.20-1.27 (m, 6H), 3.74-3.81 (m, 2H), 3.99-4.01 (m, 1H), 4.21-4.25 (m, 1H), 4.37-4.38 (m, 1H), 4.81-4.85 (m, 1H), 5.58 (dd, J = 8.0, 4.0 Hz, 1H), 5.82-5.95 (m, 1H), 5.96-6.09 (m, 1H), 6.10-6.13 (m, 1H), 7.18 (dd, J = 12.0, 8.0 Hz, 2H), 7.53-7.57 (m, 3H), 11.52 (s, 1H)
55	4-F-Ph	H	H	Me	c-Hex	¹ H NMR (DMSO-d ₆): δ 1.20-1.44 (m, 12H), 1.60-1.71 (m, 4H), 3.75-4.02 (m, 2H), 3.94-4.02 (m, 1H), 4.19-4.26 (m, 2H), 4.59-4.61 (m, 1H), 5.57 (t, J = 8.4 Hz, 1H), 5.85-6.06 (m, 3H), 7.17-7.23 (m, 4H), 7.54 (d, J = 8.4 Hz, 1H), 11.50 (s, 1H); MS, m/e 587.92 (M+1) ⁺
56	4-Br-Ph	H	H	Mc	c-Hex	¹ H NMR (400MHz, DMSO-d ₆): δ 1.18-1.46 (m, 12H), 1.61-1.69 (m, 4H), 3.75-3.82 (m, 2H), 3.95-4.08 (m, 1H), 4.25-4.28 (m, 1H), 4.38 (s, 1H), 4.60-4.62 (m, 1H), 5.56-5.60 (m, 1H), 5.82-5.95 (m, 1H), 6.02-6.20 (m, 2H), 7.09-7.20 (m, 2H), 7.53-7.57 (m, 3H), 11.52 (s, 1H) MS, m/e 650.0 (M+3) ⁺
57	Ph	H	H	Et	i-Pr	¹ H NMR (400MHz, DMSO-d ₆): δ 0.75-0.82 (m, 3H), 1.12-1.26 (m, 9H), 1.52-1.59 (m, 2H), 3.55-3.68 (m, 1H), 3.72-3.85 (m, 1H), 3.95-4.08 (m, 1H), 4.18-4.28 (m, 1H), 4.32-4.41 (m, 1H), 4.83-4.86 (m, 1H), 5.55 (m, J = 7.6Hz, 1H), 5.99-6.04 (m, 2H), 6.05-6.10 (m, 1H), 7.14-7.21 (m, 3H), 7.33-7.37 (m, 2H), 7.52-7.54 (m, 1H), 11.53 (s, 1H); MS, m/e 566.07 (M+23) ⁺
58	Ph	H	H	Et	c-Hex	¹ H NMR (400MHz, DMSO-d ₆): δ 0.75-0.88 (m, 3H), 1.26-1.46 (m, 9H), 1.52-1.69 (m, 6H), 3.60-3.63 (m, 1H), 3.72-3.90 (m, 1H), 4.02-4.03 (m, 1H), 4.24-4.27 (m, 1H), 4.37-4.38 (m, 1H), 4.63-4.65 (m, 1H), 5.55 (dd, J = 8.0Hz, 4.4Hz, 1H), 5.80-5.95 (m, 1H), 6.00-6.07 (m, 2H), 7.15-7.22 (m, 3H), 7.34-7.38 (m, 2H), 7.54 (d, J = 8.0Hz, 1H), 11.55 (s, 1H); MS, m/e 584.01 (M+1) ⁺ , 606.17 (M+23) ⁺
59	4-F-Ph	H	H	Et	c-Hex	¹ H NMR (DMSO-d ₆): δ 0.75-0.84 (m, 3H), 1.24 (d, J = 22.8Hz, 3H), 1.29-1.47 (m, 6H), 1.51-1.70 (m, 6H), 3.59-3.66 (m, 1H), 3.77-3.84 (m, 1H), 3.98-4.04 (m, 1H), 4.21-4.27 (m, 1H), 4.34-4.41 (m, 1H), 4.60-4.65 (m, 1H), 5.56-5.60 (m, 1H), 5.84-5.90 (m, 1H), 6.00-6.08 (m, 2H), 7.20-7.24 (m, 4H), 7.56 (d, J = 8.0Hz, 1H), 11.49 (s, 1H); MS, m/e 602.00 (M+1) ⁺
60	Ph	H	H	Mc	F-CH ₂ -CH ₂ -	¹ H NMR (DMSO-d ₆): δ 1.18-1.25 (m, 6H), 3.71-3.89 (m, 2H), 3.92-3.99 (m, 1H), 4.19-4.27 (m, 4H), 4.48-4.61 (m, 2H), 3.94-3.98 (m, 2H), 4.11-4.23 (m, 4H), 5.47-5.52 (m, 1H), 6.01-6.11 (m, 1H), 5.90-6.14

Ex.	R ¹	R ²	R ^{3a}	R ^{3b}	R ⁴	NMR/MS
						(m, 2H), 7.15-7.21 (m, 3H), 7.32-7.36 (m, 2H), 7.46-7.57 (m, 1H), 11.49 (s, 1H); MS, <i>m/e</i> 533.86 (M+1) ⁺
61	Ph	H	H	Me	F ₂ CH-CH ₂ -	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.17-1.24 (m, 6H), 3.67-3.81 (m, 1H), 3.89-3.98 (m, 2H), 4.21-4.36 (m, 4H), 5.48-5.53 (m, 1H), 5.82-6.05 (m, 2H), 6.18-6.22 (m, 2H), 7.15-7.20 (m, 3H), 7.32-7.36 (m, 2H), 7.51 (s, 1H), 11.50 (s, 1H); MS, <i>m/e</i> 551.92 (M+1) ⁺
62	Ph	H	H	Me	(CF ₃) ₂ -CH-	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.13-1.29 (m, 6H), 3.67-3.81 (m, 1H), 3.94-4.32 (m, 4H), 5.47 (t, <i>J</i> = 8 Hz, 1H), 5.82-6.01 (m, 2H), 6.33-6.36 (m, 1H), 6.70-6.78 (m, 1H), 7.09-7.15 (m, 3H), 7.28-7.32 (m, 2H), 7.43-7.46 (m, 1H), 11.44 (s, 1H); MS, <i>m/e</i> 637.90 (M+1) ⁺
63	Ph	H	H	Me	(CH ₂ F) ₂ -CH-	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.20-1.29 (m, 6H), 3.70-3.90 (m, 1H), 3.91-4.12 (m, 2H), 4.20-4.33 (m, 1H), 4.35-4.48 (m, 1H), 4.52-4.55 (m, 2H), 4.63-4.67 (m, 2H), 5.20-5.35 (m, 1H), 5.56 (t, <i>J</i> = 8.4 Hz, 1H), 5.80-5.95 (m, 1H), 5.95-6.10 (m, 1H), 6.18-6.21 (m, 1H), 7.18-7.23 (m, 3H), 7.35-7.39 (m, 2H), 7.54 (s, 1H), 11.55 (s, 1H); MS, <i>m/e</i> 565.98 (M+1) ⁺
64	Ph	H	H	Me	c-Pr-CH ₂ -	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.20-0.24 (m, 2H), 0.47-0.48 (m, 2H), 0.76-0.84 (m, 3H), 1.03-1.05 (m, 1H), 1.23 (dd, <i>J</i> = 22.4, 6.8 Hz, 3H), 1.55-1.60 (m, 2H), 3.61-3.68 (m, 1H), 3.81-3.89 (m, 3H), 3.98-4.03 (m, 1H), 4.23-4.29 (m, 1H), 4.35-4.41 (m, 1H), 5.56-6.00 (m, 1H), 5.88-5.91 (m, 1H), 6.04-6.10 (m, 2H), 7.20-7.24 (m, 4H), 7.55 (d, <i>J</i> = 7.6 Hz, 1H), 11.53 (s, 1H); MS, <i>m/e</i> 573.17 (M+1) ⁺
65	Ph	H	H	Et	c-Pen	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.75-0.83 (m, 3H), 1.20-1.28 (m, 3H), 1.49-1.63 (m, 8H), 1.76-1.80 (m, 2H), 3.58-3.60 (m, 1H), 3.70-3.82 (m, 1H), 3.98-4.05 (m, 1H), 4.24-4.26 (m, 1H), 4.37-4.42 (m, 1H), 5.03 (s, 1H), 5.54-5.57 (m, 1H), 5.90-6.00 (m, 1H), 6.02-6.07 (m, 2H), 7.15-7.22 (m, 3H), 7.35-7.39 (m, 2H), 7.55 (d, <i>J</i> = 8.0 Hz, 1H), 11.55 (s, 1H); MS, <i>m/e</i> 570.03 (M+1) ⁺

*R² and R^{3b} together are -(CH₂)₃- as derived from L-proline

The purification procedure by Prep-HPLC:

Crude products were dissolved in methanol. Injection volumes of these solutions
5 were 5 mL.

The preparative HPLC system including 2 sets of Gilson 306 pumps, a Gilson 156 UV/Vis detector, a Gilson 215 injector & fraction collector, with Unipoint control software. A Ymc 25×30×2 mm column was used. The mobile phase was HPLC grade

water (A), and HPLC grade acetonitrile (B). Fractions were collected into 100*15mm glass tubes.

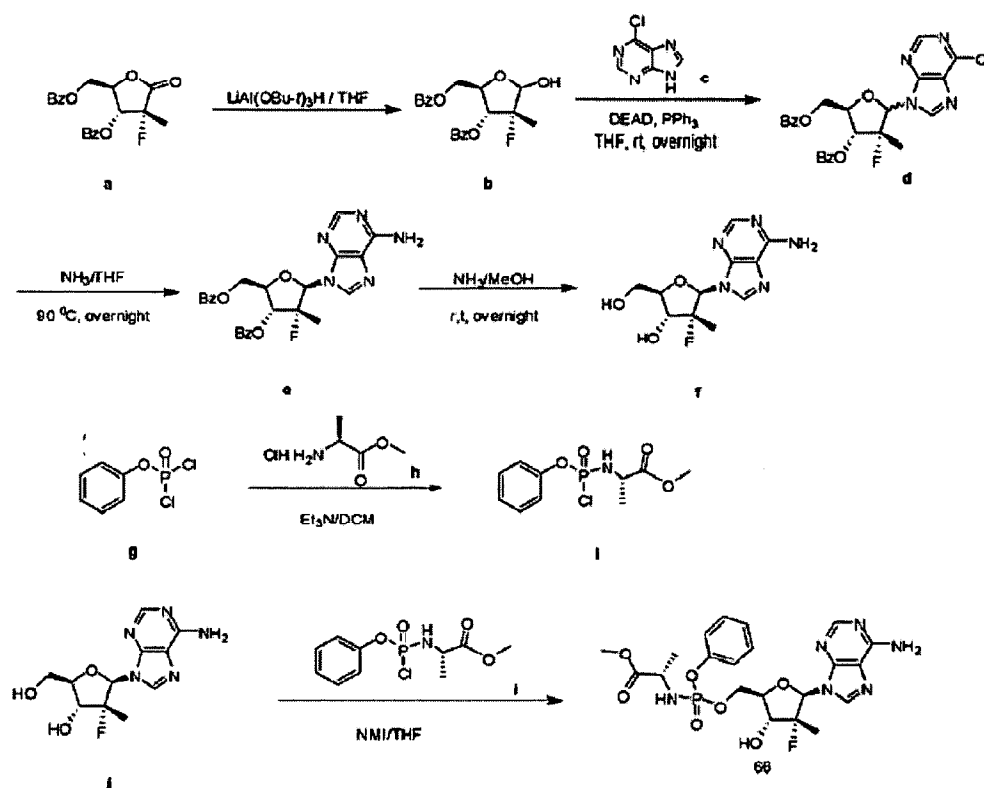
- 5 HPLC gradient is shown in Table 1. Once the gradient was selected, acetonitrile solution was injected into HPLC system, and then fractions collected according to UV peaks. After the separation, each glass tubes were run MS test to collect the desired compounds. The fractions with target MS were combined in a well-weighted flask. Most of acetonitrile was removed under reduce pressure and the remaining solution was freeze-dried to give desired compound.

10 Table 1:

Preparative HPLC gradient			
Time (min)	Flow rate (mL/min)	% A	% B
0	15	90	10
30	15	60	40

Preparation of Example 66

Scheme



Preparation of compound (b)

To a solution of compound a (1 g, 2.69 mmol) in anhydrous THF (30 mL) was added dropwise 1 M solution of $\text{LiAl}(\text{OBu-}t)_3\text{H}$ in THF (2.69 mL, 2.69 mmol) at $-20\text{ }^\circ\text{C}$.

- 5 The reaction mixture was stirred for 2-3 h at the same temperature. EtOAc (100 mL) was added followed by saturated NH_4Cl solution (10 mL) and reaction mixture was slowly brought to room temperature. Reaction mixture was extracted with EtOAc and washed with 1N HCl and water. Combined organic phase was evaporated to give 0.8 g of crude compound b as transparent oil, which was used directly for next reaction.

10 Preparation of compound (d)

To a solution of compound b (0.8 g, 2.1 mmol), compound c (0.45 g, 2.5 mmol) and Ph_3P (0.56 g, 2.1 mmol) in anhydrous THF (20 mL) under nitrogen atmosphere was added DEAD (1.8 mL). The reaction mixture was stirred at room temperature overnight. The reaction solution was concentrated under reduce pressure. The residue was separated

by preparative layer chromatography (hexanes:EtOAc = 3:1) to give crude compound d (0.8 g). The crude compound d was used to the next step without further purification.

Preparation of compound (e)

Compound d (0.8 g, 1.57 mmol) was dissolved in THF (2 mL) and THF saturated with ammonia (5 mL) was then added to this solution. The reaction mixture was heated to 90 °C overnight. After 18 hours, the solution was cooled to room temperature by ice water, then the solvent was removed under reduced pressure and the residue was purified by column to give compound e (0.75 g) for the next step.

Preparation of compound (f)

Compound e (0.5 g, 1.01 mmol) was dissolved in methanol (2 mL) and methanol was saturated with ammonia (5 mL) was then added to this solution. The reaction mixture was stirred at room temperature overnight. After 18 hours, the solvent was removed under reduced pressure and the residue was purified by column to give crude compound f (0.15 g) for the next step.

Preparation of compound (i)

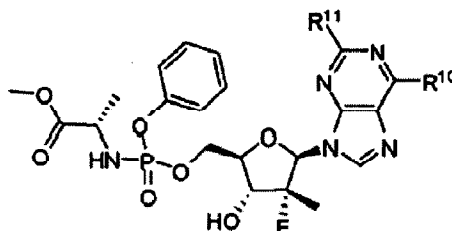
A solution of triethylamine (1.07 g, 10.6 mmol) in anhydrous dichloromethane (15 mL) was added dropwise to a solution of compound g (1.16 g, 5.3 mmol) and compound h (1.31 g, 5.3 mmol) in dichloromethane (10 mL) with vigorous stirring at -78 °C over a period of 2 hours. After completion of addition, the reaction temperature was allowed to warm to room temperature gradually and stirred over night. Then the solvent was removed under vacuum and anhydrous ether 20 mL was added and the precipitated salt was filtered and the precipitate was washed with ether. The combined organic phase was concentrated to give the colorless oil of compound i (1.0 g).

Preparation of Compound 66

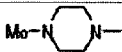
To a solution of compound j (0.1 g, 0.35 mmol) dissolved in 10 mL of anhydrous THF, stirred and added 0.4g NMI till the solution became clear, added compound i (0.8 g, 2.89 mmol) in 10 mL THF dropwise, stirred at r.t. overnight. Compound purity and identification was confirmed by LCMS. The solvent was evaporated and purified by Prep-HPLC to afford 66. (25 mg, Yield: 13.6%). ¹H NMR (DMSO-*d*₆) δ 1.08 (d, *J* = 22.8 Hz, 3H), 1.17-1.24 (m, 3H), 3.50-3.52 (m, 3H), 3.78-3.83 (m, 1H), 4.10-4.13 (m,

1H), 4.24-4.44 (m, 2H), 5.85-5.92 (m, 1H), 6.01-6.11 (m, 1H), 6.2-6.27 (m, 1H), 7.08-7.19 (m, 4H), 7.31-7.38 (m, 3H), 8.15 (s, 1H), 8.26 (s, 1H); MS, *m/e* 525 (M+1)⁺.

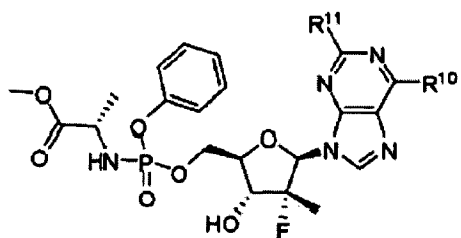
- 5 Example numbers 67-74, identified below, were prepared using similar procedures disclosed for Example 66, above.



Example	R ¹¹	R ¹⁰	NMR/MS
67	OH	NH ₂	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.06-1.13 (m, 3H), 1.20-1.24 (m, 3H), 3.27-3.33 (m, 3H), 3.56 (s, 1H), 3.82-3.88 (m, 1H), 4.07-4.13 (m, 1H), 4.25-4.40 (m, 2H), 5.85-5.87 (m, 1H), 5.98-6.09 (m, 2H), 6.59 (s, 32H), 7.14-7.37 (m, 3H), 7.35-7.37 (m, 2H), 7.79 (d, <i>J</i> =7.2 Hz, 1H), 10.69 (s, 1H); MS, <i>m/e</i> 541 (M+1) ⁺ ;
68	NH ₂	NH ₂	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.07 (d, <i>J</i> =22.8 Hz, 3H), 1.19 (d, <i>J</i> =7.2 Hz, 3H), 3.51 (s, 3H), 3.62 (s, 1H), 3.75-3.81 (m, 1H), 4.05-4.11 (m, 1H), 4.27-4.42 (m, 2H), 5.79-5.83 (m, 1H), 5.92 (s, 2H), 6.00-6.09 (m, 2H), 6.75 (s, 2H), 7.08-7.17 (m, 3H), 7.31-7.35 (m, 2H), 7.78 (s, 1H); MS, <i>m/e</i> 540 (M+1) ⁺ ;
69	NH ₂	c-Pentyl-NH-	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.05 (d, <i>J</i> =22.8 Hz, 3H), 1.09-1.19 (m, 3H), 1.48 (s, 4H), 1.66 (s, 1H), 1.86 (s, 1H), 3.54 (d, <i>J</i> =14 Hz, 3H), 3.65 (s, 1H), 4.25-4.43 (m, 4H), 5.71-5.82 (m, 1H), 5.94-6.04 (m, 4H), 7.11-7.24 (m, 3H), 7.26-7.34 (m, 2H), 7.77 (d, <i>J</i> =3.6 Hz, 1H); MS, <i>m/e</i> 608 (M+1) ⁺
70	NH ₂		¹ H NMR (DMSO- <i>d</i> ₆) δ 1.07 (d, <i>J</i> =22.4 Hz, 3H), 2.35-2.38 (m, 2H), 3.54 (d, <i>J</i> =9.2 Hz, 3H), 3.59-3.62 (m, 2H), 3.65 (s, 1H), 3.75-3.82 (m, 1H), 4.01-4.13 (m, 2H), 4.22-4.40 (m, 6H), 5.75-5.85 (m, 1H), 6.00-6.07 (m, 4H), 7.15-7.21 (m, 3H), 7.32-7.35 (m, 2H), 7.79 (d, <i>J</i> =4.0 Hz, 1H); MS, <i>m/e</i> 580 (M+1) ⁺
71	NH ₂	Et ₂ N-	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.06-1.28 (m, 12H), 3.55 (d, <i>J</i> =4.8 Hz, 3H), 3.79-3.87 (m, 4H), 4.07-4.12 (m, 2H), 4.29-4.42 (m,

Example	R ¹¹	R ¹⁰	NMR/MS
			3H), 5.75-5.82 (m, 1H), 5.94 (s, 2H), 6.04-6.10 (m, 2H), 7.14-7.22 (m, 3H), 7.31-7.37 (m, 2H), 7.82 (d, <i>J</i> =4.4 Hz, 1H); MS, <i>m/e</i> 596 (M+1) ⁺
72	NH ₂	n-Propyl-NH-	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.84 (t, <i>J</i> =7.2 Hz, 3H), 1.01-1.01 (m, 3H), 1.09-1.12 (m, 3H), 1.51-1.56 (m, 2H), 3.48 (d, <i>J</i> =15.2 Hz, 3H), 3.79-3.82 (m, 1H), 4.04-4.05 (m, 1H), 4.27-4.38 (m, 3H), 5.72-5.79 (m, 1H), 5.98-6.04 (m, 4H), 7.13-7.20 (m, 3H), 7.26-7.32 (m, 2H), 7.76 (d, <i>J</i> =5.2 Hz, 1H); MS, <i>m/e</i> 582 (M+1) ⁺
73	NH ₂	c-Butyl-NH-	¹ H NMR (DMSO- <i>d</i> ₆) δ 1.02-1.08 (m, 3H), 1.18 (d, <i>J</i> =4.8 Hz, 3H), 1.44-1.61 (m, 2H), 2.02-2.17 (m, 4H), 3.51 (d, <i>J</i> =10.8 Hz, 3H), 3.78-3.83 (m, 1H), 4.03-4.06 (m, 1H), 4.27-4.38 (m, 2H), 4.53-4.62 (m, 1H), 5.68-5.79 (m, 1H), 5.95-6.04 (m, 4H), 7.11-7.18 (m, 3H), 7.29-7.35 (m, 2H), 7.51-7.58 (m, 1H), 7.78 (d, <i>J</i> =5.2 Hz, 1H); MS, <i>m/e</i> 594 (M+1) ⁺
74	NH ₂	Mo-N 	¹ H NMR (DMSO- <i>d</i> ₆) δ 0.97-1.20 (m, 6H), 2.18 (s, 3H), 2.19 (s, 4H), 3.43-3.47 (m, 3H), 3.75 (s, 1H), 4.01-4.06 (m, 4H), 4.22-4.35 (m, 3H), 5.69-5.75 (m, 1H), 5.98-6.05 (m, 3H), 7.09-7.15 (m, 3H), 7.25-7.29 (m, 2H), 7.77 (d, <i>J</i> =3.6 Hz, 1H); MS, <i>m/e</i> 623 (M+1) ⁺

Example numbers 75-80 are prepared using similar procedures disclosed for Example 66, above.



Example	R ¹¹	R ¹⁰
75	H	n-propyl-NH-
76	H	c-Butyl-NH-
77	H	c-Pentyl-NH-
78	H	
79	H	
80	H	

EXAMPLE 81

Certain exemplified compounds were obtained as mixture of diastereomers because of the chirality at phosphorous. The diastereomers were separated on a Chiralpak-AS-H (2 X 25 cm) column under Supercritical Fluid Chromatography (SFC) conditions using 20% methanol in carbon dioxide as solvent. The absolute stereochemistry of the P-chiral center of the diastereomers were not determined. However, chromatographic resolution of these two diastereomers provides for isomers that are characterized as fast eluting and slow eluting isomers. Some examples are shown below.

Compound	EC90 (uM)
Example 15 (Diastereomeric mixture)	0.86
Fast Moving isomer of Example 15	1.35
Slow Moving isomer of Example 15	0.26

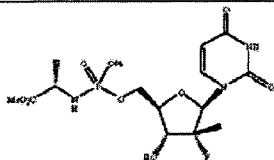
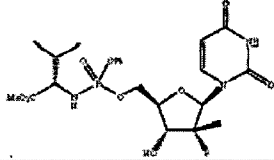
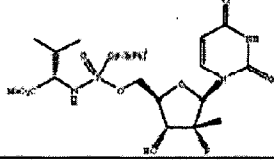
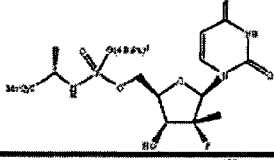
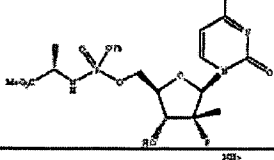
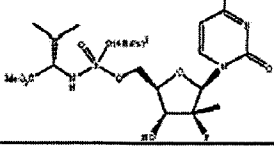
Compound	EC90 (uM)
Example 39 (Diastereomeric mixture)	0.47
Fast Moving isomer of Example 39	0.78
Slow Moving isomer of Example 39	0.02
Example 49 (Diastereomeric mixture)	0.126
Fast Moving isomer of Example 49	0.03
Slow Moving isomer of Example 49	5.78

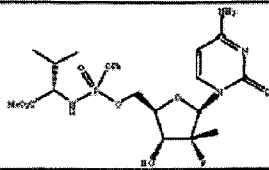
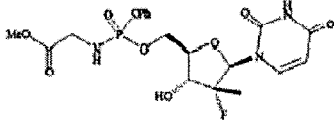
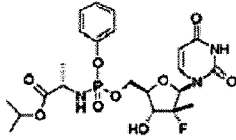
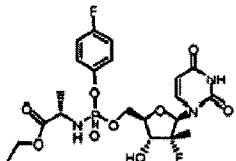
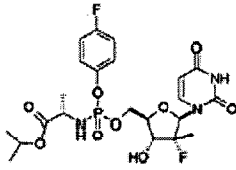
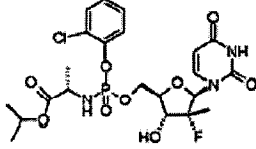
EXAMPLE 82

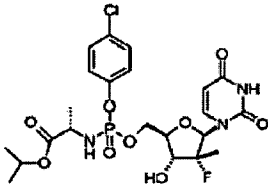
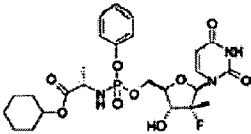
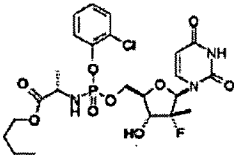
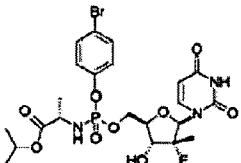
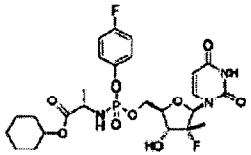
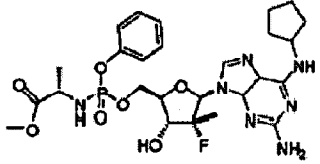
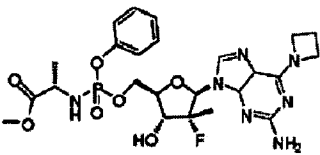
HCV replicon assay. HCV replicon RNA-containing Huh7 cells (clone A cells; Apath, LLC, St. Louis, Mo.) were kept at exponential growth in Dulbecco's modified Eagle's medium (high glucose) containing 10% fetal bovine serum, 4 mM L-glutamine and 1 mM sodium pyruvate, 1× nonessential amino acids, and G418 (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', and antisense, 5'-TTCCGCAGACCACTATGG-3'; probe, 5'-FAM-CCTCCAGGACCCCCCTCCC-TAMRA-3').

To express the antiviral effectiveness of a compound, the threshold RT-PCR cycle of the test compound was subtracted from the average threshold RT-PCR cycle of the no-drug control (ΔC_{tHCV}). A ΔC_t of 3.3 equals a 1-log 10 reduction (equal to the 90%

effective concentration [EC₉₀]) in replicon RNA levels. The cytotoxicity of the test compound could also be expressed by calculating the ΔC_{tRNA} values. The $\Delta\Delta C_t$ specificity parameter could then be introduced ($\Delta C_{tHCV} - \Delta C_{tRNA}$), in which the levels of HCV RNA are normalized for the rRNA levels and calibrated against the no-drug control.

Ex #	Compound	Log10 Reduction at 50 μ M	EC90 (μ M)
5		-1.21	3.0
6		-0.45	ND
7		0.31	ND
8		-1.48	2.11
10		-1.25	19.15
11		-0.55	ND

Ex #	Compound	Log10 Reduction at 50µM	EC90 (µM)
12		0.31	ND
15		ND	0.86
25		-2.22	0.39
27		-2.25	0.66
28		-2.16	0.75
36		-1.64	21.9

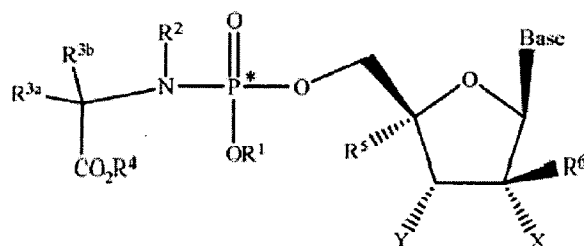
Ex #	Compound	Log10 Reduction at 50μM	EC90 (μM)
39		-1.78	0.47
49		-2.69	0.126
53		-1.33	<0.3
54		-1.55	0.57
55		-2.38	<0.3
69		-2.25	< 0.3
70		-2.25	<0.3

¹(4-BrPh): 4-bromo-phenyl.

The entire contents of U.S. Provisional Application Nos. 60/909,315, filed March 30, 2007, and 60/982,309, filed October 24, 2007, are hereby incorporated by reference
5 in the present application so far as needed to supplement the present disclosure and/or rectify any errors. Moreover, the patent and non-patent references disclosed herein are incorporated by reference. In the event that the incorporated patent and non-patent reference contains a term that conflicts with a term disclosed in either one of the two Provisional Applications or the present application text, the meaning of the term
10 contained in the present application text and the two Provisional Applications controls provided that the overall meaning of the incorporated subject matter is not lost.

We claim:

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



I

wherein

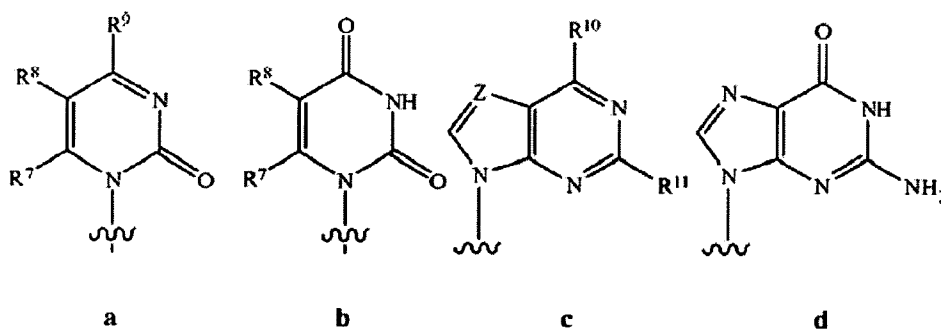
- (a) R^1 is hydrogen, n-alkyl; branched alkyl; cycloalkyl; or aryl, which includes, but is not limited to, phenyl or naphthyl, where phenyl or naphthyl are optionally substituted with at least one of C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, F, Cl, Br, I, nitro, cyano, C_{1-6} haloalkyl, $-N(R^1)_2$, C_{1-6} acylamino, $-NHSO_2C_{1-6}$ alkyl, $-SO_2N(R^1)_2$, COR^1 , and $-SO_2C_{1-6}$ alkyl; (R^1 is independently hydrogen or alkyl, which includes, but is not limited to, C_{1-20} alkyl, C_{1-10} alkyl, or C_{1-6} alkyl, R^1 is $-OR^1$ 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, $-CH_2SH$, $-(CH_2)_2S(O)_2Me$, $-(CH_2)_3NHC(=NH)NH_2$, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, $-(CH_2)_cCOR^3$, 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 $(CH_2)_r$ 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 ,
5 $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, 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 ,
10 $CH_2C(O)NH_2$, 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 $-N(R^{3'})_2$;
- 15 (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,
20 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;
- 25 (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), OC₁₋₁₀ haloalkyl, O(aminoacyl), O(C₁₋₁₀ acyl), O(C₁₋₄ alkyl), O(C₂₋₄ alkenyl),
S(C₁₋₄ acyl), S(C₁₋₄ alkyl), S(C₂₋₄ alkynyl), S(C₂₋₄ alkenyl), SO(C₁₋₄ acyl), SO(C₁₋₄ alkyl),
SO(C₂₋₄ alkynyl), SO(C₂₋₄ alkenyl), SO₂(C₁₋₄ acyl), SO₂(C₁₋₄ alkyl), SO₂(C₂₋₄ alkynyl),
SO₂(C₂₋₄ alkenyl), OS(O)₂(C₁₋₄ acyl), OS(O)₂(C₁₋₄ alkyl), OS(O)₂(C₂₋₄ alkenyl), NH₂,
5 NH(C₁₋₄ alkyl), NH(C₂₋₄ alkenyl), NH(C₂₋₄ alkynyl), NH(C₁₋₄ acyl), N(C₁₋₄ alkyl)₂, N(C₁₋₄
alkyl)₂, wherein alkyl, alkynyl, alkenyl and vinyl are optionally substituted by N₃, CN,
one to three halogen (Cl, Br, F, I), NO₂, C(O)O(C₁₋₄ alkyl), C(O)O(C₁₋₄ alkyl), C(O)O(C₂₋₄
alkynyl), C(O)O(C₂₋₄ alkenyl), O(C₁₋₄ acyl), O(C₁₋₄ alkyl), O(C₂₋₄ alkenyl), S(C₁₋₄ acyl),
S(C₁₋₄ alkyl), S(C₂₋₄ alkynyl), S(C₂₋₄ alkenyl), SO(C₁₋₄ acyl), SO(C₁₋₄ alkyl), SO(C₂₋₄
10 alkynyl), SO(C₂₋₄ alkenyl), SO₂(C₁₋₄ acyl), SO₂(C₁₋₄ alkyl), SO₂(C₂₋₄ alkynyl), SO₂(C₂₋₄
alkenyl), OS(O)₂(C₁₋₄ acyl), OS(O)₂(C₁₋₄ alkyl), OS(O)₂(C₂₋₄ alkenyl), NH₂, NH(C₁₋₄
alkyl), NH(C₂₋₄ alkenyl), NH(C₂₋₄ alkynyl), NH(C₁₋₄ acyl), N(C₁₋₄ alkyl)₂, N(C₁₋₄ acyl)₂;

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

15



wherein

Z is N or CR¹²;

R⁷, R⁸, R⁹, R¹⁰, and R¹¹ are independently H, F, Cl, Br, I, OH, OR', SH, SR', NH₂,
20 NHR', NR'₂, lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower
alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-

C₆ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂, CH=CHCO₂H, or CH=CHCO₂R',

wherein R' is an optionally substituted alkyl, which includes, but is not limited to,
5 an optionally substituted C₁₋₂₀ alkyl, an optionally substituted C₁₋₁₀ alkyl, an optionally substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted alkynyl of C₂-C₆, an optionally substituted lower alkenyl of C₂-C₆, or optionally substituted acyl, which includes but is not limited to C(O) alkyl, C(O)(C₁₋₂₀ alkyl), C(O)(C₁₋₁₀ alkyl), or C(O)(lower alkyl) or alternatively, in the instance of NR'₂, each R'
10 comprise at least one C atom that are joined to form a heterocycle comprising at least two carbon atoms; and

R¹² is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', NH₂, NHR', NR'₂, NO₂ lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-C₆,
15 halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂, CH=CHCO₂H, or CH=CHCO₂R'; with the proviso that when base is represented by the structure c with R¹¹ being hydrogen, R¹² is not a: (i) -C≡C-H, (ii) -C=CH₂, or (iii) -NO₂.

2. A compound its stereoisomer, salt, hydrate, solvate, or crystalline form
20 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);

25 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-methylbutyric acid methyl ester);

30 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-methylbutyric 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 N⁴-(*N,N*-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-C-methylcytidine;
- 10 2'-Deoxy-2'-fluoro-2'-C-methylcytidine 5'-(phenyl methoxy-alanyl phosphate
- 5 (((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}-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-butylric acid methyl ester);
- 10 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-butylric acid methyl ester;
- 15 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;
- 20 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 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;
- 25 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;
- 30 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;
- 35 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;
- 40 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;
- 45 20 (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;
- 21 (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino}-propionic acid methyl ester;
- 22 (S)-2-{(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid methyl ester;

- 23 (S)-2-[(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid methyl ester;
- 24 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid sec-butyl ester;
- 25 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid isopropyl ester;
- 26 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid butyl ester;
- 27 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid ethyl ester;
- 28 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;
- 29 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid benzyl ester;
- 30 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;
- 31 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid benzyl ester;
- 32 (S)-2-[(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 33 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino]-propionic acid isopropyl ester;
- 34 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid butyl ester;
- 35 (S)-2-[(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid ethyl ester;
- 36 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid isopropyl ester;
- 37 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid benzyl ester;

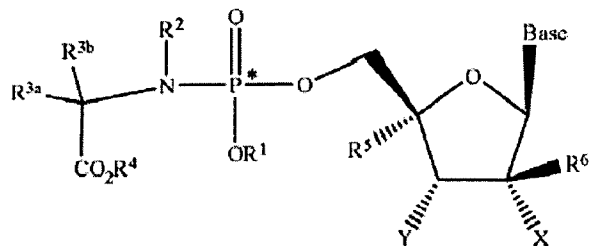
- 38 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid pentyl ester;
- 39 (S)-2-[(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester;
- 40 (S)-2-[(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;
- 41 (S)-2-[(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;
- 42 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid butyl ester;
- 43 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino}-propionic acid benzyl ester;
- 44 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-butyric acid methyl ester;
- 45 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 4-fluoro-benzyl ester;
- 46 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid butyl ester;
- 47 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid 3-methyl-butyl ester;
- 48 (S)-2-[(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid ethyl ester;
- 49 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid cyclohexyl ester;
- 50 (R)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;
- 51 (R)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;
- 52 (R)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;

- 53 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 5 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;
- 10 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;
- 15 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;
- 20 60 (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]-butyric acid isopropyl ester;
- 25 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;
- 30 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;
- 35 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;
- 40 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;
- 5 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;
- 10 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;
- 15 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-yl]-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid methyl ester;
- 20 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;
- 25 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;
- 30 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
- 35 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.
- 40

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

by formula I:



I

wherein

- 5 (a) R¹ 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 C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, F, Cl, Br, I, nitro, cyano, C₁₋₆ haloalkyl, -N(R¹)₂, C₁₋₆ acylamino, -NHSO₂C₁₋₆ alkyl, -SO₂N(R¹)₂, COR¹, and -SO₂C₁₋₆ alkyl; (R¹ is independently hydrogen or alkyl, which includes, but is not limited to, C₁₋₂₀ alkyl, C₁₋₁₀ alkyl, or C₁₋₆ alkyl, R¹ is -OR¹ or -N(R¹)₂);
- (b) R² is hydrogen, C₁₋₁₀ alkyl, R³ᵃ or R³ᵇ and R² together are (CH₂)_n so as to form a cyclic ring that includes the adjoining N and C atoms, C(O)CR³ᵃR³ᵇNHR¹, where n is 2 to 4 and R¹, R³ᵃ, and R³ᵇ;
- 15 (c) R³ᵃ and R³ᵇ are (i) independently selected from hydrogen, C₁₋₁₀ alkyl, cycloalkyl, -(CH₂)_c(NR³)₂, C₁₋₆ hydroxyalkyl, -CH₂SH, -(CH₂)₂S(O)_dMe, -(CH₂)₃NHC(=NH)NH₂, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, -(CH₂)_cCOR³, aryl and aryl C₁₋₃ alkyl, said aryl groups optionally substituted with a group selected from hydroxyl, C₁₋₁₀ alkyl, C₁₋₆ alkoxy, halogen, nitro and cyano; (ii) R³ᵃ and R³ᵇ both are C₁₋₆ alkyl; (iii) R³ᵃ and R³ᵇ together are (CH₂)_f so as to form a spiro ring; (iv) R³ᵃ is hydrogen and R³ᵇ and R² together are (CH₂)_n so as to form a cyclic ring that includes the adjoining N and C atoms (v) R³ᵃ is hydrogen and R³ᵃ and R² together are (CH₂)_n so as to form a cyclic ring that includes the adjoining N and C atoms, where c is 1
- 20

- 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 , $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, -
- 5 $CH_2CH_2CH_2NHC(NH)NH_2$, 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 , $CH_2CH_2C(O)NH_2$, $CH_2CH_2CH_2CH_2NH_2$, -
- 10 $CH_2CH_2CH_2NHC(NH)NH_2$, 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,
- 15 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,
- 20 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;

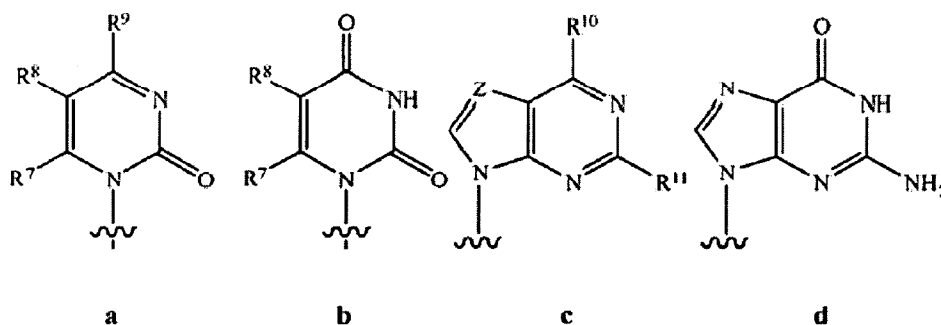
(f) R^6 is H, CH_3 , CH_2F , CHF_2 , CF_3 , F, or CN;

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

- 25 (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(C₂₋₄ alkynyl), SO(C₂₋₄ alkenyl), SO₂(C₁₋₄ acyl), SO₂(C₁₋₄ alkyl), SO₂(C₂₋₄ alkynyl),
 SO₂(C₂₋₄ alkenyl), OS(O)₂(C₁₋₄ acyl), OS(O)₂(C₁₋₄ alkyl), OS(O)₂(C₂₋₄ alkenyl), NH₂,
 NH(C₁₋₄ alkyl), NH(C₂₋₄ alkenyl), NH(C₂₋₄ alkynyl), NH(C₁₋₄ acyl), N(C₁₋₄ alkyl)₂, N(C₁₋₄
 5 one to three halogen (Cl, Br, F, I), NO₂, C(O)O(C₁₋₄ alkyl), C(O)O(C₁₋₄ alkyl), C(O)O(C₂₋₄
 4 alkynyl), C(O)O(C₂₋₄ alkenyl), O(C₁₋₄ acyl), O(C₁₋₄ alkyl), O(C₂₋₄ alkenyl), S(C₁₋₄ acyl),
 S(C₁₋₄ alkyl), S(C₂₋₄ alkynyl), S(C₂₋₄ alkenyl), SO(C₁₋₄ acyl), SO(C₁₋₄ alkyl), SO(C₂₋₄
 alkynyl), SO(C₂₋₄ alkenyl), SO₂(C₁₋₄ acyl), SO₂(C₁₋₄ alkyl), SO₂(C₂₋₄ alkynyl), SO₂(C₂₋₄
 alkenyl), OS(O)₂(C₁₋₄ acyl), OS(O)₂(C₁₋₄ alkyl), OS(O)₂(C₂₋₄ alkenyl), NH₂, NH(C₁₋₄
 10 alkyl), NH(C₂₋₄ alkenyl), NH(C₂₋₄ alkynyl), NH(C₁₋₄ acyl), N(C₁₋₄ alkyl)₂, N(C₁₋₄ acyl)₂;

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



15 wherein

Z is N or CR¹²,

R⁷, R⁸, R⁹, R¹⁰, and R¹¹ are independently H, F, Cl, Br, I, OH, OR', SH, SR', NH₂,
 NHR', NR'₂, lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower
 alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-
 20 C₆ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-

C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂, CH=CHCO₂H, or CH=CHCO₂R',

wherein R' is an optionally substituted alkyl, which includes, but is not limited to, an optionally substituted C₁₋₂₀ alkyl, an optionally substituted C₁₋₁₀ alkyl, an optionally substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted alkynyl of C₂-C₆, an optionally substituted lower alkenyl of C₂-C₆, or optionally substituted acyl, which includes but is not limited to C(O) alkyl, C(O)(C₁₋₂₀ alkyl), C(O)(C₁₋₁₀ 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

R¹² is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', NH₂, NHR', NR'₂, NO₂ lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂, CH=CHCO₂H, or CH=CHCO₂R'; with the proviso that when base is represented by the structure c with R¹¹ being hydrogen, R¹² is not a: (i) -C≡C-H, (ii) -C=CH₂, or (iii) -NO₂.

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-methylbutyric 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);
- 5 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);
- 10 9 N¹-(N,N-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-C-methylcytidine;
- 10 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]-phenoxy-phosphorylamino)-propionic acid methyl ester);
- 15 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);
- 20 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;
- 25 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;
- 30 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;
- 35 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;
- 40 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;
- 45

- 21 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid methyl ester;
- 22 (S)-2-[(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid methyl ester;
- 23 (S)-2-[(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid methyl ester;
- 24 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid sec-butyl ester;
- 25 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid isopropyl ester;
- 26 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid butyl ester;
- 27 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid ethyl ester;
- 28 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;
- 29 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid benzyl ester;
- 30 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;
- 31 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid benzyl ester;
- 32 (S)-2-[(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 33 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino]-propionic acid isopropyl ester;
- 34 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid butyl ester;
- 35 (S)-2-[(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid ethyl ester;

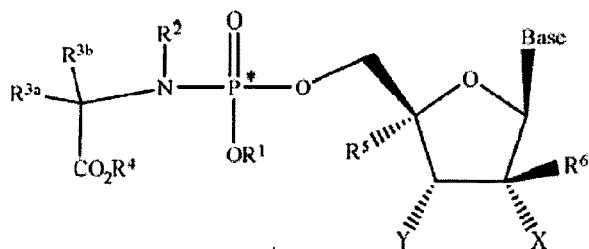
- 36 (S)-2-((2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid isopropyl ester;
- 37 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-(4-methoxy-phenoxy)-phosphorylamino)-propionic acid benzyl ester;
- 38 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-propionic acid pentyl ester;
- 39 (S)-2-((4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid isopropyl ester;
- 40 (S)-2-((4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid butyl ester;
- 41 (S)-2-((4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid ethyl ester;
- 42 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-p-tolylloxy-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-tolylloxy-phosphorylamino)-propionic acid benzyl ester;
- 44 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-butyric acid methyl ester;
- 45 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-propionic acid 4-fluoro-benzyl ester;
- 46 (S)-2-((2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid butyl ester;
- 47 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-propionic acid 3-methyl-butyl ester;
- 48 (S)-2-((2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid ethyl ester;
- 49 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-propionic acid cyclohexyl ester;
- 50 (R)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-propionic acid butyl ester;

- 51 (R)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester;
- 52 (R)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid benzyl ester;
- 53 (S)-2-([(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 54 (S)-2-([(4-Bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid isopropyl ester;
- 55 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;
- 56 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-bromo-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;
- 57 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-butyric acid isopropyl ester;
- 58 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-butyric acid cyclohexyl ester;
- 59 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino)-butyric acid cyclohexyl ester;
- 60 (S)-2-([(4-Chloro-phenoxy)-[(2R,3R,4R,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;
5 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;
10 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;
15 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;
20 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-yl]-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid methyl ester;
25 75 (2S)-methyl 2-[[[(2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(propylamino)-9H-purin-9-yl)tetrahydrofuran-2-ylmethoxy](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-ylmethoxy](phenoxy)phosphorylamino]propanoate;
30 77 (2S)-methyl 2-[[[(2R,3R,4R,5R)-5-(6-(cyclopentylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-ylmethoxy](phenoxy)phosphorylamino]propanoate;
35 78 (2S)-methyl 2-[[[(2R,3R,4R,5R)-5-(6-(aziridin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-ylmethoxy](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-ylmethoxy](phenoxy)phosphorylamino]propanoate; and
40 80 (2S)-methyl 2-[[[(2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-ylmethoxy](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.

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



I

wherein

10 (a) R¹ 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 C₁-₆ alkyl, C₂-₆ alkenyl, C₂-₆ alkynyl, C₁-₆ alkoxy, F, Cl, Br, I, nitro, cyano, C₁-₆ haloalkyl, -N(R¹)₂, C₁-₆ acylamino, -NHSO₂C₁-₆ alkyl, -SO₂N(R¹)₂, COR¹', and -SO₂C₁-₆ alkyl; (R¹' is independently hydrogen or alkyl, 15 which includes, but is not limited to, C₁-₂₀ alkyl, C₁-₁₀ alkyl, or C₁-₆ alkyl, R¹' is -OR¹ or -N(R¹)₂);

(b) R² is hydrogen, C₁-₁₀ alkyl, R³ᵃ or R³ᵇ and R² together are (CH₂)ₙ so as to form a cyclic ring that includes the adjoining N and C atoms, C(O)CR³ᵃR³ᵇNHR¹, where n is 2 to 4 and R¹, R³ᵃ, and R³ᵇ;

20 (c) R³ᵃ and R³ᵇ are (i) independently selected from hydrogen, C₁-₁₀ alkyl, cycloalkyl, -(CH₂)₆(NR³)₂, C₁-₆ hydroxyalkyl, -CH₂SH, -(CH₂)₂S(O)₄Me, -(CH₂)₃NHC(=NH)NH₂, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, -(CH₂)₆COR³', aryl and aryl C₁-₃ alkyl, said aryl groups optionally substituted with a

- group selected from hydroxyl, C₁₋₁₀ alkyl, C₁₋₆ alkoxy, halogen, nitro and cyano; (ii) R^{3a} and R^{3b} both are C₁₋₆ alkyl; (iii) R^{3a} and R^{3b} together are (CH₂)_f so as to form a spiro ring; (iv) R^{3a} is hydrogen and R^{3b} and R² together are (CH₂)_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 R² together are (CH₂)_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 C₁₋₆ alkyl and R^{3''} is -OR' or -N(R^{3'})₂; (vi) R^{3a} is H and R^{3b} is H, CH₃, CH₂CH₃, CH(CH₃)₂, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, CH₂Ph, CH₂-indol-3-yl, -CH₂CH₂SCH₃, CH₂CO₂H, CH₂C(O)NH₂, CH₂CH₂COOH, CH₂CH₂C(O)NH₂, CH₂CH₂CH₂CH₂NH₂, -CH₂CH₂CH₂NHC(NH)NH₂, CH₂-imidazol-4-yl, CH₂OH, CH(OH)CH₃, CH₂((4'-OH)-Ph), CH₂SH, or lower cycloalkyl; or (viii) R^{3a} is CH₃, -CH₂CH₃, CH(CH₃)₂, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, CH₂Ph, CH₂-indol-3-yl, -CH₂CH₂SCH₃, CH₂CO₂H, CH₂C(O)NH₂, CH₂CH₂COOH, CH₂CH₂C(O)NH₂, CH₂CH₂CH₂CH₂NH₂, -CH₂CH₂CH₂NHC(NH)NH₂, CH₂-imidazol-4-yl, CH₂OH, CH(OH)CH₃, CH₂((4'-OH)-Ph), CH₂SH, or lower cycloalkyl and R^{3b} is H, where R^{3'} is independently hydrogen or alkyl, which includes, but is not limited to, C₁₋₂₀ alkyl, C₁₋₁₀ alkyl, or C₁₋₆ alkyl, R^{3''} is -OR' or -N(R^{3'})₂;

- (d) R⁴ is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkyl optionally substituted with a lower alkyl, alkoxy, di(lower alkyl)-amino, or halogen, C₁₋₁₀ haloalkyl, C₃₋₁₀ cycloalkyl, cycloalkyl alkyl, cycloheteroalkyl, aminoacyl, aryl, such as phenyl, heteroaryl, such as, pyridinyl, substituted aryl, or substituted heteroaryl;

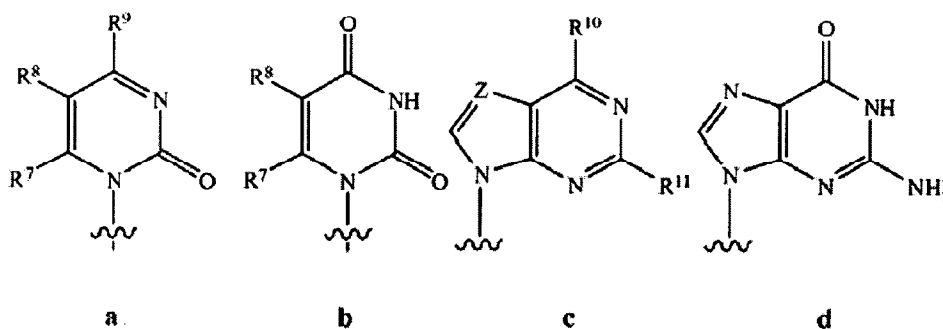
- (e) R⁵ is H, a lower alkyl, CN, vinyl, O-(lower alkyl), hydroxyl lower alkyl, i.e., -(CH₂)_pOH, where p is 1 -6, including hydroxyl methyl (CH₂OH), CH₂F, N₃, CH₂CN, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, alkyne (optionally substituted), or halogen, including F, Cl, Br, or I, with the provisos that when X is OH, base is cytosine and R⁶ is H, R⁵ cannot be N₃ and when X is OH, R⁶ is CH₃ or CH₂F and B is a purine base, R⁵ cannot be H;

- (f) R⁶ is H, CH₃, CH₂F, CHF₂, CF₃, F, or CN;

- (g) X is H, OH, F, OMe, halogen, NH₂, or N₃;

(h) Y is OH, H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, vinyl, N₃, CN, Cl, Br, F, I, NO₂, OC(O)O(C₁₋₄ alkyl), OC(O)O(C₁₋₄ alkyl), OC(O)O(C₂₋₄ alkynyl), OC(O)O(C₂₋₄ alkenyl), OC₁₋₁₀ haloalkyl, O(aminoacyl), O(C₁₋₁₀ acyl), O(C₁₋₄ alkyl), O(C₂₋₄ alkenyl), S(C₁₋₄ acyl), S(C₁₋₄ alkyl), S(C₂₋₄ alkynyl), S(C₂₋₄ alkenyl), SO(C₁₋₄ acyl), SO(C₁₋₄ alkyl), SO(C₂₋₄ alkynyl), SO(C₂₋₄ alkenyl), SO₂(C₁₋₄ acyl), SO₂(C₁₋₄ alkyl), SO₂(C₂₋₄ alkynyl), SO₂(C₂₋₄ alkenyl), OS(O)₂(C₁₋₄ acyl), OS(O)₂(C₁₋₄ alkyl), OS(O)₂(C₂₋₄ alkenyl), NH₂, NH(C₁₋₄ alkyl), NH(C₂₋₄ alkenyl), NH(C₂₋₄ alkynyl), NH(C₁₋₄ acyl), N(C₁₋₄ alkyl)₂, N(C₁₋₁₈ acyl)₂, wherein alkyl, alkynyl, alkenyl and vinyl are optionally substituted by N₃, CN, one to three halogen (Cl, Br, F, I), NO₂, C(O)O(C₁₋₄ alkyl), C(O)O(C₁₋₄ alkyl), C(O)O(C₂₋₄ alkynyl), C(O)O(C₂₋₄ alkenyl), O(C₁₋₄ acyl), O(C₁₋₄ alkyl), O(C₂₋₄ alkenyl), S(C₁₋₄ acyl), S(C₁₋₄ alkyl), S(C₂₋₄ alkynyl), S(C₂₋₄ alkenyl), SO(C₁₋₄ acyl), SO(C₁₋₄ alkyl), SO(C₂₋₄ alkynyl), SO(C₂₋₄ alkenyl), SO₂(C₁₋₄ acyl), SO₂(C₁₋₄ alkyl), SO₂(C₂₋₄ alkynyl), SO₂(C₂₋₄ alkenyl), OS(O)₂(C₁₋₄ acyl), OS(O)₂(C₁₋₄ alkyl), OS(O)₂(C₂₋₄ alkenyl), NH₂, NH(C₁₋₄ alkyl), NH(C₂₋₄ alkenyl), NH(C₂₋₄ alkynyl), NH(C₁₋₄ acyl), N(C₁₋₄ alkyl)₂, N(C₁₋₄ acyl)₂;

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



wherein

Z is N or CR¹²;

R^7 , R^8 , R^9 , R^{10} , and R^{11} are independently H, F, Cl, Br, I, OH, OR', SH, SR', NH₂, NHR', NR'₂, lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-C₆ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂, CH=CHCO₂H, or CH=CHCO₂R',

wherein R' is an optionally substituted alkyl, which includes, but is not limited to, an optionally substituted C₁₋₂₀ alkyl, an optionally substituted C₁₋₁₀ alkyl, an optionally substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted alkynyl of C₂-C₆, an optionally substituted lower alkenyl of C₂-C₆, or optionally substituted acyl, which includes but is not limited to C(O) alkyl, C(O)(C₁₋₂₀ alkyl), C(O)(C₁₋₁₀ 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', NH₂, NHR', NR'₂, NO₂ lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂, CH=CHCO₂H, or CH=CHCO₂R'; with the proviso that when base is represented by the structure c with R¹¹ being hydrogen, R¹² is not a: (i) -C≡C-H, (ii) -C=CH₂, or (iii) -NO₂.

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);

30 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-butyrac 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-butyrac 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 N⁴-(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]-phenoxy-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-butyrac 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-butyrac 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;
- 5 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;
- 10 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;
- 15 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;
- 20 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;
- 25 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 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;
- 35 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;
- 40 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;
- 45

- 35 (S)-2-((3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid ethyl ester;
- 36 (S)-2-((2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid isopropyl ester;
- 37 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-(4-methoxy-phenoxy)-phosphorylamino)-propionic acid benzyl ester;
- 38 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-propionic acid pentyl ester;
- 39 (S)-2-((4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid isopropyl ester;
- 40 (S)-2-((4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid butyl ester;
- 41 (S)-2-((4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid ethyl ester;
- 42 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-p-tolyloxy-phosphorylamino)-propionic acid butyl ester;
- 43 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-p-tolyloxy-phosphorylamino)-propionic acid benzyl ester;
- 44 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-butyric acid methyl ester;
- 45 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-propionic acid 4-fluoro-benzyl ester;
- 46 (S)-2-((2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid butyl ester;
- 47 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-propionic acid 3-methyl-butyl ester;
- 48 (S)-2-((2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino)-propionic acid ethyl ester;
- 49 (S)-2-(((2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy)-phenoxy-phosphorylamino)-propionic acid cyclohexyl ester;

- 50 (R)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid butyl ester;
- 5 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;
- 10 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;
- 15 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;
- 20 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;
- 25 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;
- 30 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;
- 35 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;
- 40 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;
- 45

- 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;
- 5 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;
- 10 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;
- 15 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;
- 20 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;
- 25 74 (S)-2-[[[(2R,3R,4R,5R)-5-[2-Amino-6-(4-methyl-piperazin-1-yl)-purin-9-yl]-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid methyl ester;
- 30 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;
- 35 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;
- 40 79 (2S)-methyl 2-((((2R,3R,4R,5R)-4-fluoro-3-hydroxy-4-methyl-5-(6-(piperidin-1-yl)-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate; and

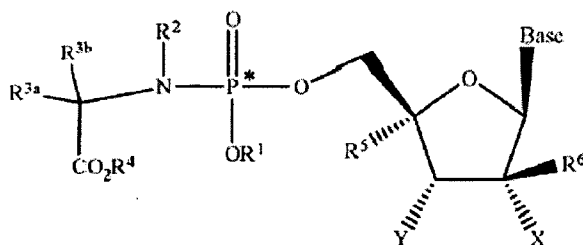
80 (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate

5 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.

10 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) R¹ 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 C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, F, Cl, Br, I, nitro, cyano, C₁₋₆ haloalkyl, -N(R^{1'})₂, C₁₋₆ acylamino, -NHSO₂C₁₋₆ alkyl, -SO₂N(R^{1'})₂, COR^{1'}, and -SO₂C₁₋₆ alkyl; (R^{1'} is independently hydrogen or alkyl,

which includes, but is not limited to, C₁₋₂₀ alkyl, C₁₋₁₀ alkyl, or C₁₋₆ alkyl, R^{1'} is -OR' or -N(R^{1'})₂;

(b) R² is hydrogen, C₁₋₁₀ alkyl, R^{3a} or R^{3b} and R² together are (CH₂)_n so as to form a cyclic ring that includes the adjoining N and C atoms, C(O)CR^{3a}R^{3b}NHR¹, where
5 n is 2 to 4 and R¹, R^{3a}, and R^{3b};

(c) R^{3a} and R^{3b} are (i) independently selected from hydrogen, C₁₋₁₀ alkyl, cycloalkyl, -(CH₂)_c(NR^{3'})₂, C₁₋₆ hydroxyalkyl, -CH₂SH, -(CH₂)₂S(O)_dMe, -(CH₂)₃NHC(=NH)NH₂, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, -(CH₂)_eCOR^{3'}, aryl and aryl C₁₋₃ alkyl, said aryl groups optionally substituted with a
10 group selected from hydroxyl, C₁₋₁₀ alkyl, C₁₋₆ alkoxy, halogen, nitro and cyano; (ii) R^{3a} and R^{3b} both are C₁₋₆ alkyl; (iii) R^{3a} and R^{3b} together are (CH₂)_f so as to form a spiro ring; (iv) R^{3a} is hydrogen and R^{3b} and R² together are (CH₂)_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 R² together are (CH₂)_n so as to form a cyclic ring that includes the adjoining N and C atoms, where c is 1
15 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 C₁₋₆ alkyl and R^{3'} is -OR' or -N(R^{3'})₂; (vi) R^{3a} is H and R^{3b} is H, CH₃, CH₂CH₃, CH(CH₃)₂, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, CH₂Ph, CH₂-indol-3-yl, -CH₂CH₂SCH₃, CH₂CO₂H, CH₂C(O)NH₂, CH₂CH₂COOH, CH₂CH₂C(O)NH₂, CH₂CH₂CH₂CH₂NH₂, -CH₂CH₂CH₂NHC(NH)NH₂, CH₂-imidazol-4-yl, CH₂OH, CH(OH)CH₃, CH₂((4'-OH)-Ph), CH₂SH, or lower cycloalkyl; or (viii) R^{3a} is CH₃, -CH₂CH₃, CH(CH₃)₂, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, CH₂Ph, CH₂-indol-3-yl, -CH₂CH₂SCH₃, CH₂CO₂H, CH₂C(O)NH₂, CH₂CH₂COOH, CH₂CH₂C(O)NH₂, CH₂CH₂CH₂CH₂NH₂, -CH₂CH₂CH₂NHC(NH)NH₂, CH₂-imidazol-4-yl, CH₂OH, CH(OH)CH₃, CH₂((4'-OH)-Ph), CH₂SH, or lower cycloalkyl and R^{3b} is H, where R^{3'} is independently hydrogen or
20 alkyl, which includes, but is not limited to, C₁₋₂₀ alkyl, C₁₋₁₀ alkyl, or C₁₋₆ alkyl, R^{3'} is -OR' or -N(R^{3'})₂;

(d) R⁴ is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkyl optionally substituted with a lower alkyl, alkoxy, di(lower alkyl)-amino, or halogen, C₁₋₁₀ haloalkyl, C₃₋₁₀ cycloalkyl,

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

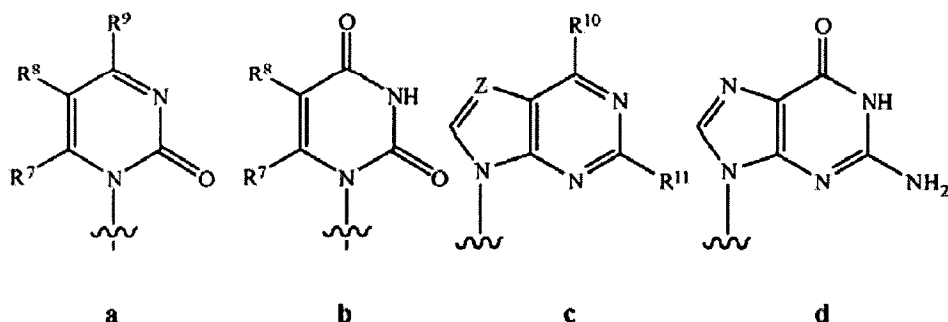
- (e) R^5 is H, a lower alkyl, CN, vinyl, O-(lower alkyl), hydroxyl lower alkyl, i.e., $-(CH_2)_pOH$, where p is 1-6, including hydroxyl methyl (CH_2OH), CH_2F , N_3 ,
5 CH_2CN , CH_2NH_2 , CH_2NHCH_3 , $CH_2N(CH_3)_2$, alkyne (optionally substituted), or halogen, including F, Cl, Br, or I, with the 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;

- 10 (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),
15 $SO(C_{2-4}$ 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),
20 $S(C_{1-4}$ 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) $_2$;

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



wherein

Z is N or CR¹²;

R⁷, R⁸, R⁹, R¹⁰, and R¹¹ are independently H, F, Cl, Br, I, OH, OR', SH, SR', NH₂,
 5 NHR', NR'₂, lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower
 alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-
 C₆ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-
 C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR',
 CONR'₂, CH=CHCO₂H, or CH=CHCO₂R',

10 wherein R' is an optionally substituted alkyl, which includes, but is not limited to,
 an optionally substituted C₁₋₂₀ alkyl, an optionally substituted C₁₋₁₀ alkyl, an optionally
 substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted
 alkynyl of C₂-C₆, an optionally substituted lower alkenyl of C₂-C₆, or optionally
 substituted acyl, which includes but is not limited to C(O) alkyl, C(O)(C₁₋₂₀ alkyl),
 15 C(O)(C₁₋₁₀ 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

R¹² is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', NH₂, NHR', NR'₂,
 NO₂ lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower alkenyl
 20 of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-C₆,
 halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-C₆, halogenated (F,
 Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂,

$\text{CH}=\text{CHCO}_2\text{H}$, or $\text{CH}=\text{CHCO}_2\text{R}^1$; with the proviso that when base is represented by the structure c with R^{11} being hydrogen, R^{12} is not a: (i) $-\text{C}\equiv\text{C}-\text{H}$, (ii) $-\text{C}=\text{CH}_2$, or (iii) $-\text{NO}_2$.

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

5 administering a therapeutically effective amount of a compound, its stereoisomer, salt, hydrate, solvate, or crystalline form thereof, selected from among

10 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-butyrac acid methyl ester);

15 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-butyrac acid methyl ester);

20 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;

25 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]-phenoxy-phosphorylamino}-propionic acid methyl ester);

30 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-butyrac acid methyl ester);

35 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-butyrac acid methyl ester;

40 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 15 {[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-acetic acid methyl ester;

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

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

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

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

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

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

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

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

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

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

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

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

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

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

- 30 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;
- 5 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;
- 10 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;
- 15 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;
- 20 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;
- 25 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;
- 30 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;
- 35 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;
- 40 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

- 45 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid 4-fluoro-benzyl ester;
- 46 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 47 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid 3-methyl-butyl ester;
- 48 (S)-2-[(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid ethyl ester;
- 49 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid cyclohexyl ester;
- 50 (R)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid butyl ester;
- 51 (R)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid isopropyl ester;
- 52 (R)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid benzyl ester;
- 53 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 54 (S)-2-[(4-Bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid isopropyl ester;
- 55 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;
- 56 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-bromo-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;
- 57 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-butyric acid isopropyl ester;
- 58 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-butyric acid cyclohexyl ester;
- 59 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-butyric acid cyclohexyl ester;

- 60 (S)-2-[(4-Chloro-phenoxy)-[(2R,3R,4R,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-yl]-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;

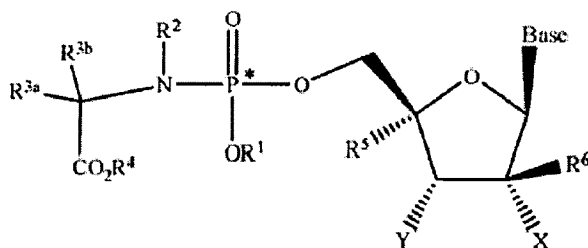
78 (2S)-methyl 2-((((2R,3R,4R,5R)-5-(6-(aziridin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate;

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.

20

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



I

25

wherein

(a) R¹ 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 C₁-₆ alkyl, C₂-₆ alkenyl, C₂-₆ alkynyl, C₁-₆ alkoxy, F, Cl, Br, I, nitro, cyano, C₁-₆ haloalkyl, -N(R¹')₂, C₁-₆ acylamino, -NHSO₂C₁-₆ alkyl, -SO₂N(R¹')₂, COR¹'', and -SO₂C₁-₆ alkyl; (R¹' is independently hydrogen or alkyl,

30

which includes, but is not limited to, C₁₋₂₀ alkyl, C₁₋₁₀ alkyl, or C₁₋₆ alkyl, R^{1'} is -OR' or -N(R^{1'})₂;

(b) R² is hydrogen, C₁₋₁₀ alkyl, R^{3a} or R^{3b} and R² together are (CH₂)_n so as to form a cyclic ring that includes the adjoining N and C atoms, C(O)CR^{3a}R^{3b}NHR¹, where
5 n is 2 to 4 and R¹, R^{3a}, and R^{3b};

(c) R^{3a} and R^{3b} are (i) independently selected from hydrogen, C₁₋₁₀ alkyl, cycloalkyl, -(CH₂)_c(NR^{3'})₂, C₁₋₆ hydroxyalkyl, -CH₂SH, -(CH₂)₂S(O)_dMe, -(CH₂)₃NHC(=NH)NH₂, (1H-indol-3-yl)methyl, (1H-imidazol-4-yl)methyl, -(CH₂)_eCOR^{3'}, aryl and aryl C₁₋₃ alkyl, said aryl groups optionally substituted with a
10 group selected from hydroxyl, C₁₋₁₀ alkyl, C₁₋₆ alkoxy, halogen, nitro and cyano; (ii) R^{3a} and R^{3b} both are C₁₋₆ alkyl; (iii) R^{3a} and R^{3b} together are (CH₂)_f so as to form a spiro ring; (iv) R^{3a} is hydrogen and R^{3b} and R² together are (CH₂)_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 R² together are (CH₂)_n so as to form a cyclic ring that includes the adjoining N and C atoms, where c is 1
15 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 C₁₋₆ alkyl and R^{3'} is -OR' or -N(R^{3'})₂; (vi) R^{3a} is H and R^{3b} is H, CH₃, CH₂CH₃, CH(CH₃)₂, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, CH₂Ph, CH₂-indol-3-yl, -CH₂CH₂SCH₃, CH₂CO₂H, CH₂C(O)NH₂, CH₂CH₂COOH, CH₂CH₂C(O)NH₂, CH₂CH₂CH₂CH₂NH₂, -CH₂CH₂CH₂NHC(NH)NH₂, CH₂-imidazol-4-yl, CH₂OH, CH(OH)CH₃, CH₂((4'-OH)-Ph), CH₂SH, or lower cycloalkyl; or (viii) R^{3a} is CH₃, -CH₂CH₃, CH(CH₃)₂, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, CH₂Ph, CH₂-indol-3-yl, -CH₂CH₂SCH₃, CH₂CO₂H, CH₂C(O)NH₂, CH₂CH₂COOH, CH₂CH₂C(O)NH₂, CH₂CH₂CH₂CH₂NH₂, -CH₂CH₂CH₂NHC(NH)NH₂, CH₂-imidazol-4-yl, CH₂OH, CH(OH)CH₃, CH₂((4'-OH)-Ph), CH₂SH, or lower cycloalkyl and R^{3b} is H, where R^{3'} is independently hydrogen or
20 alkyl, which includes, but is not limited to, C₁₋₂₀ alkyl, C₁₋₁₀ alkyl, or C₁₋₆ alkyl, R^{3'} is -OR' or -N(R^{3'})₂;

(d) R⁴ is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkyl optionally substituted with a lower alkyl, alkoxy, di(lower alkyl)-amino, or halogen, C₁₋₁₀ haloalkyl, C₃₋₁₀ cycloalkyl,

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

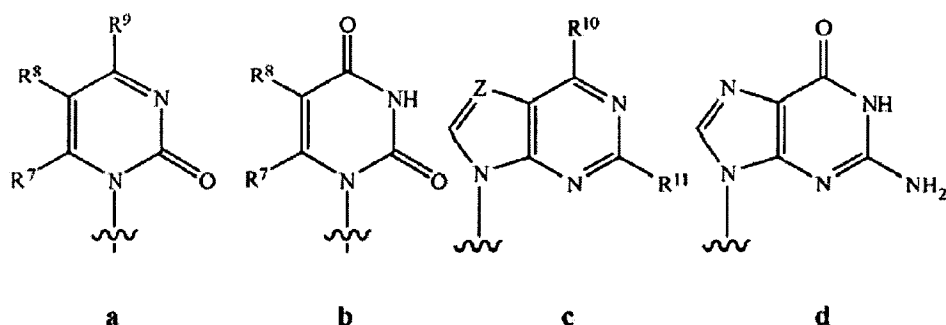
- (e) R^5 is H, a lower alkyl, CN, vinyl, O-(lower alkyl), hydroxyl lower alkyl, i.e., $-(CH_2)_pOH$, where p is 1 -6, including hydroxyl methyl (CH_2OH), CH_2F , N_3 ,
5 CH_2CN , CH_2NH_2 , CH_2NHCH_3 , $CH_2N(CH_3)_2$, alkyne (optionally substituted), or halogen, including F, Cl, Br, or I, with the 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;

- 10 (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),
15 $SO(C_{2-4}$ 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),
20 $S(C_{1-4}$ 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) $_2$;

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



wherein

Z is N or CR¹²;

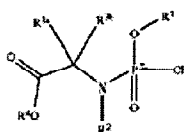
- R⁷, R⁸, R⁹, R¹⁰, and R¹¹ are independently H, F, Cl, Br, I, OH, OR', SH, SR', NH₂,
 5 NHR', NR'₂, lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower
 alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-
 C₆ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-
 C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR',
 CONR'₂, CH=CHCO₂H, or CH=CHCO₂R',
 10 wherein R' is an optionally substituted alkyl, which includes, but is not limited to,
 an optionally substituted C₁₋₂₀ alkyl, an optionally substituted C₁₋₁₀ alkyl, an optionally
 substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted
 alkynyl of C₂-C₆, an optionally substituted lower alkenyl of C₂-C₆, or optionally
 substituted acyl, which includes but is not limited to C(O) alkyl, C(O)(C₁₋₂₀ alkyl),
 15 C(O)(C₁₋₁₀ 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

- R¹² is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', NH₂, NHR', NR'₂,
 NO₂ lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower alkenyl
 20 of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-C₆,
 halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-C₆, halogenated (F,
 Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂,

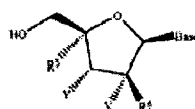
$\text{CH}=\text{CHCO}_2\text{H}$, or $\text{CH}=\text{CHCO}_2\text{R}^1$; with the proviso that when base is represented by the structure c with R^{11} being hydrogen, R^{12} is not a: (i) $-\text{C}\equiv\text{C}-\text{H}$, (ii) $-\text{C}=\text{CH}_2$, or (iii) $-\text{NO}_2$;

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-butiric 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-butiric 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 N⁴-(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]-phenoxy-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-butiric 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;
- 5 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)-
10 phosphorylamino]-propionic acid benzyl ester;
- 15 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]-
15 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;
- 20 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]-
25 propionic acid butyl ester;
- 20 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)-
30 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;
- 35 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]-
40 propionic acid sec-butyl ester;
- 25 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)-
45 phosphorylamino]-propionic acid butyl ester;

- 27 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid ethyl ester;
- 28 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;
- 29 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid benzyl ester;
- 30 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;
- 31 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid benzyl ester;
- 32 (S)-2-[(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 33 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy]-phosphorylamino]-propionic acid isopropyl ester;
- 34 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid butyl ester;
- 35 (S)-2-[(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid ethyl ester;
- 36 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid isopropyl ester;
- 37 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid benzyl ester;
- 38 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid pentyl ester;
- 39 (S)-2-[(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid isopropyl ester;
- 40 (S)-2-[(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 41 (S)-2-[(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid ethyl ester;

- 42 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino]-propionic acid butyl ester;
- 43 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyloxy-phosphorylamino]-propionic acid benzyl ester;
- 44 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-butyric acid methyl ester;
- 45 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid 4-fluoro-benzyl ester;
- 46 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 47 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid 3-methyl-butyl ester;
- 48 (S)-2-[(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid ethyl ester;
- 49 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid cyclohexyl ester;
- 50 (R)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid butyl ester;
- 51 (R)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid isopropyl ester;
- 52 (R)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid benzyl ester;
- 53 (S)-2-[(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 54 (S)-2-[(4-Bromo-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid isopropyl ester;
- 55 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;
- 56 (S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-bromo-phenoxy)-phosphorylamino]-propionic acid cyclohexyl ester;

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

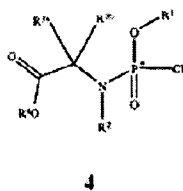
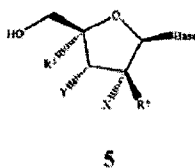
78 (2S)-methyl 2-[[[(2R,3R,4R,5R)-5-(6-(aziridin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy](phenoxy)phosphorylamino]propanoate;

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

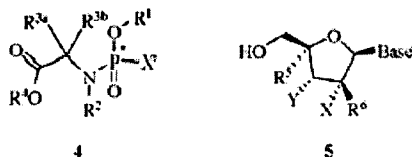
said process comprising:

reacting a substituted phosphochloridate compound 4 with a nucleoside analog 5



11. 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



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

CH₂CH₂CH₂NHC(NH)NH₂, CH₂-imidazol-4-yl, CH₂OH, CH(OH)CH₃, CH₂((4'-OH)-Ph), CH₂SH, or lower cycloalkyl; or (viii) R^{3a} is CH₃, -CH₂CH₃, CH(CH₃)₂,

CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, CH₂Ph, CH₂-indol-3-yl, -CH₂CH₂SCH₃, CH₂CO₂H, CH₂C(O)NH₂, CH₂CH₂COOH, CH₂CH₂C(O)NH₂, CH₂CH₂CH₂CH₂NH₂, -

- 5 CH₂CH₂CH₂NHC(NH)NH₂, CH₂-imidazol-4-yl, CH₂OH, CH(OH)CH₃, CH₂((4'-OH)-Ph), CH₂SH, or lower cycloalkyl and R^{3b} is H, where R³ is independently hydrogen or alkyl, which includes, but is not limited to, C₁₋₂₀ alkyl, C₁₋₁₀ alkyl, or C₁₋₆ alkyl, R^{3'} is -OR' or -N(R^{3'})₂;

- (d) R⁴ is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkyl optionally substituted with a lower alkyl, alkoxy, di(lower alkyl)-amino, or halogen, C₁₋₁₀ haloalkyl, C₃₋₁₀ cycloalkyl, 10 cycloalkyl alkyl, cycloheteroalkyl, aminoacyl, aryl, such as phenyl, heteroaryl, such as, pyridinyl, substituted aryl, or substituted heteroaryl;

- (e) R⁵ is H, a lower alkyl, CN, vinyl, O-(lower alkyl), hydroxyl lower alkyl, i.e., -(CH₂)_pOH, where p is 1-6, including hydroxyl methyl (CH₂OH), CH₂F, N₃, 15 CH₂CN, CH₂NH₂, CH₂NHCH₃, CH₂N(CH₃)₂, alkyne (optionally substituted), or halogen, including F, Cl, Br, or I, with the provisos that when X is OH, base is cytosine and R⁶ is H, R⁵ cannot be N₃ and when X is OH, R⁶ is CH₃ or CH₂F and B is a purine base, R⁵ cannot be H;

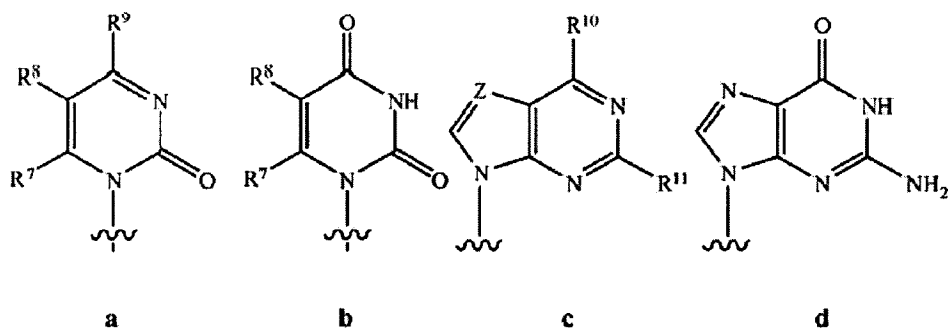
(f) R⁶ is H, CH₃, CH₂F, CHF₂, CF₃, F, or CN;

- 20 (g) X is H, OH, F, OMe, halogen, NH₂, or N₃;

- (h) Y is OH, H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, vinyl, N₃, CN, Cl, Br, F, I, NO₂, OC(O)O(C₁₋₄ alkyl), OC(O)O(C₁₋₄ alkyl), OC(O)O(C₂₋₄ alkynyl), OC(O)O(C₂₋₄ alkenyl), OC₁₋₁₀ haloalkyl, O(aminoacyl), O(C₁₋₁₀ acyl), O(C₁₋₄ alkyl), O(C₂₋₄ alkenyl), S(C₁₋₄ acyl), S(C₁₋₄ alkyl), S(C₂₋₄ alkynyl), S(C₂₋₄ alkenyl), SO(C₁₋₄ acyl), SO(C₁₋₄ alkyl), 25 SO(C₂₋₄ alkynyl), SO(C₂₋₄ alkenyl), SO₂(C₁₋₄ acyl), SO₂(C₁₋₄ alkyl), SO₂(C₂₋₄ alkynyl), SO₂(C₂₋₄ alkenyl), OS(O)₂(C₁₋₄ acyl), OS(O)₂(C₁₋₄ alkyl), OS(O)₂(C₂₋₄ alkynyl), NH₂, NH(C₁₋₄ alkyl), NH(C₂₋₄ alkenyl), NH(C₂₋₄ alkynyl), NH(C₁₋₄ acyl), N(C₁₋₄ alkyl)₂, N(C₁₋₁₈ acyl)₂, wherein alkyl, alkynyl, alkenyl and vinyl are optionally substituted by N₃, CN,

one to three halogen (Cl, Br, F, I), NO₂, C(O)O(C₁₋₄ alkyl), C(O)O(C₁₋₄ alkyl), C(O)O(C₂₋₄ alkynyl), C(O)O(C₂₋₄ alkenyl), O(C₁₋₄ acyl), O(C₁₋₄ alkyl), O(C₂₋₄ alkenyl), S(C₁₋₄ acyl), S(C₁₋₄ alkyl), S(C₂₋₄ alkynyl), S(C₂₋₄ alkenyl), SO(C₁₋₄ acyl), SO(C₁₋₄ alkyl), SO(C₂₋₄ alkynyl), SO(C₂₋₄ alkenyl), SO₂(C₁₋₄ acyl), SO₂(C₁₋₄ alkyl), SO₂(C₂₋₄ alkynyl), SO₂(C₂₋₄ alkenyl), OS(O)₂(C₁₋₄ acyl), OS(O)₂(C₁₋₄ alkyl), OS(O)₂(C₂₋₄ alkenyl), NH₂, NH(C₁₋₄ alkyl), NH(C₂₋₄ alkenyl), NH(C₂₋₄ alkynyl), NH(C₁₋₄ acyl), N(C₁₋₄ alkyl)₂, N(C₁₋₄ acyl)₂;

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



wherein

Z is N or CR¹²;

R⁷, R⁸, R⁹, R¹⁰, and R¹¹ are independently H, F, Cl, Br, I, OH, OR', SH, SR', NH₂, NHR', NR'₂, lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-C₆ such as C≡CH, halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂, CH=CHCO₂H, or CH=CHCO₂R',

wherein R' is an optionally substituted alkyl, which includes, but is not limited to, an optionally substituted C₁₋₂₀ alkyl, an optionally substituted C₁₋₁₀ alkyl, an optionally substituted lower alkyl; an optionally substituted cycloalkyl; an optionally substituted

alkynyl of C₂-C₆, an optionally substituted lower alkenyl of C₂-C₆, or optionally substituted acyl, which includes but is not limited to C(O) alkyl, C(O)(C₁₋₂₀ alkyl), C(O)(C₁₋₁₀ 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

R¹² is an H, halogen (including F, Cl, Br, I), OH, OR', SH, SR', NH₂, NHR', NR'₂, NO₂ lower alkyl of C₁-C₆, halogenated (F, Cl, Br, I) lower alkyl of C₁-C₆, lower alkenyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkenyl of C₂-C₆, lower alkynyl of C₂-C₆, halogenated (F, Cl, Br, I) lower alkynyl of C₂-C₆, lower alkoxy of C₁-C₆, halogenated (F, Cl, Br, I) lower alkoxy of C₁-C₆, CO₂H, CO₂R', CONH₂, CONHR', CONR'₂, CH=CHCO₂H, or CH=CHCO₂R'; with the proviso that when base is represented by the structure c with R¹¹ being hydrogen, R¹² is not a: (i) -C≡C-H, (ii) -C=CH₂, or (iii) -NO₂

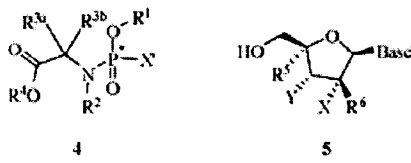
and

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

15

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



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

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

- 6 2'-Deoxy-2'-fluoro-2'-C-methyluridine 5'-(phenyl methoxy-valyl phosphate ((S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-3-methyl-butylric acid methyl ester);
- 5 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-butylric 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);
- 10 9 N⁴-(N,N-dimethylformamidinyl)-2'-deoxy-2'-fluoro-2'-C-methylcytidine;
- 10 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]-phenoxy-phosphorylamino}-propionic acid methyl ester);
- 15 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-butylric acid methyl ester);
- 20 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-butylric acid methyl ester);
- 25 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;
- 30 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 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;
- 35 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;
- 40 17 (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(naphthalen-1-yloxy)-phosphorylamino}-propionic acid methyl ester;
- 18 (S)-1-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphoryl}-pyrrolidine-2-carboxylic acid methyl ester;

- 19 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid butyl ester;
- 20 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid benzyl ester;
- 21 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid methyl ester;
- 22 (S)-2-([(4-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid methyl ester;
- 23 (S)-2-([(3,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid methyl ester;
- 24 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid sec-butyl ester;
- 25 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino)-propionic acid isopropyl ester;
- 26 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid butyl ester;
- 27 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid ethyl ester;
- 28 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;
- 29 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-fluoro-phenoxy)-phosphorylamino]-propionic acid benzyl ester;
- 30 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-(4-methoxy-phenoxy)-phosphorylamino]-propionic acid isopropyl ester;
- 31 (S)-2-([(2-Chloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid benzyl ester;
- 32 (S)-2-([(2,4-Dichloro-phenoxy)-[(2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino]-propionic acid butyl ester;
- 33 (S)-2-([(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-p-tolyl-oxy-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;
- 5 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;
- 10 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;
- 15 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;
- 20 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;
- 25 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;
- 30 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 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;
- 40 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;
- 45

- 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,4R,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-yl]-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino]-propionic acid methyl ester;
- 75 (2S)-methyl 2-[[[(2R,3R,4R,5R)-5-(6-(propylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-5-(6-(propylamino)-9H-purin-9-yl)-tetrahydrofuran-2-ylmethoxy](phenoxy)phosphorylamino]propanoate;
- 76 (2S)-methyl 2-[[[(2R,3R,4R,5R)-5-(6-(cyclobutylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydrofuran-2-ylmethoxy](phenoxy)phosphorylamino]propanoate;
- 77 (2S)-methyl 2-[[[(2R,3R,4R,5R)-5-(6-(cyclopentylamino)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydrofuran-2-ylmethoxy](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-methyl-tetrahydrofuran-2-ylmethoxy](phenoxy)phosphorylamino]propanoate;

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

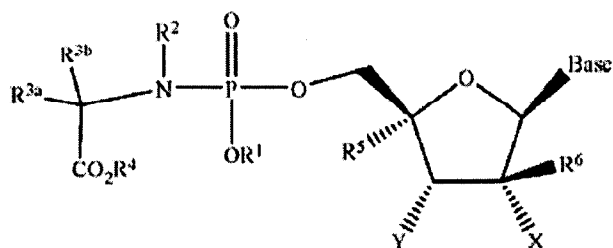
80 (2S)-methyl 2-(((2R,3R,4R,5R)-5-(6-(azetidin-1-yl)-9H-purin-9-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphorylamino)propanoate

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

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

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
5 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.

10

Electronic Patent Application Fee Transmittal				
Application Number:				
Filing Date:				
Title of Invention:		NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS		
First Named Inventor/Applicant Name:		Jinfa Du		
Filer:		Lawrence F. Rozsnyai/Sylvia Brennan		
Attorney Docket Number:		PH3080.PC7-TRK1		
Filed as Large Entity				
Track I Prioritized Examination - Nonprovisional Application under 35 USC 111(a) Filing Fees				
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
Request for Prioritized Examination	1817	1	4000	4000
Pages:				
Utility Appl Size fee per 50 sheets >100	1081	10	400	4000
Claims:				
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				9600

Electronic Acknowledgement Receipt	
EFS ID:	18798324
Application Number:	14255833
International Application Number:	
Confirmation Number:	5585
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	25000
Filer:	Lawrence F. Rozsnyai/Sylvia Brennan
Filer Authorized By:	Lawrence F. Rozsnyai
Attorney Docket Number:	PH3080.PC7-TRK1
Receipt Date:	17-APR-2014
Filing Date:	
Time Stamp:	19:19:07
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$ 9600
RAM confirmation Number	5602
Deposit Account	071250
Authorized User	
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)</p>	

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Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	TrackOne Request	PH3080PC7TRK1_Trck1_Req_as_Filed.pdf	88333 7cf02df1ac2d11f85ffa7526228171d19ff12132	no	1
Warnings:					
Information:					
2	Transmittal of New Application	PH3080PC7TRK1_Utility_Transas_Filed.pdf	90109 367dd06026a8770a696a45a73d0432f9e308f78d	no	1
Warnings:					
Information:					
3	Application Data Sheet	PH3080PC7TRK1_ADS_as_Filed.pdf	142077 4fa28c82e918448b58b2198bd536bcd0d709c3f4	no	5
Warnings:					
Information:					
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4	Power of Attorney	PH3080PC7TRK1_POA.pdf	94733 4a1ab0408cfa4827c9b6080ef84e528a4831a662	no	1
Warnings:					
Information:					
5	Oath or Declaration filed	PH3080PC7TRK1_executed_Declarations.pdf	230387 35b81b8d8f2b1b8045b98c35c18c546e5e3a11070	no	4
Warnings:					
Information:					
6	Preliminary Amendment	PH3080PC7TRK1_PremL_Amndt_As_Filed.pdf	181579 90cd50ba9e650831ae40b8d2ebc05e027ad440bb	no	7
Warnings:					
Information:					
7	Information Disclosure Statement (IDS) Form (SB08)	PH3080PC7TRK1_IDS_as_Filed.pdf	1947858 6bd0ed830094e8656acca26875809b6ed64db4d8	no	74
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					

8	Specification	PH3080PC7TRK1_Spec_as_File d.pdf	19642756 682be8b943956afb6cf0263974df053a4c8b2715	no	679
Warnings:					
Information:					
9	Claims	PH3080PC7TRK1_Claims_as_Fil ed.pdf	3552591 e82386e4705e66cabb936f00dc5f687522af98af	no	56
Warnings:					
Information:					
10	Abstract	PH3080PC7TRK1_Abstrect_as_Fi led.pdf	22231 6e50cdf158461c22e8de99829bbed0cec19r4vNR6	no	1
Warnings:					
Information:					
11	Fee Worksheet (SB06)	fee-info.pdf	38549 106650fcf1e5f00f4bc8cfad177cb211f58fa bc	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			26031203		
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>					

**CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION
UNDER 37 CFR 1.102(e) (Page 1 of 1)**

First Named Inventor:	Jinfa DU	Nonprovisional Application Number (if known):	
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS		

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.

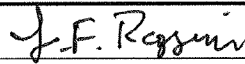
1. The processing fee set forth in 37 CFR 1.17(i)(1), the prioritized examination fee set forth in 37 CFR 1.17(c), and if not already paid, the publication fee set forth in 37 CFR 1.18(d) have been filed with the request. The basic filing fee, search fee, examination fee, and any required excess claims and application size fees are filed with the request or have been already been paid.
2. The application contains or is amended to contain no more than four independent claims and no more than thirty total claims, and no multiple dependent claims.
3. The applicable box is checked below:

I. ☒ Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)

- i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web.
---OR---
- (b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.
- ii. The executed inventor's oath or declaration is filed with the application. (37 CFR 1.63 and 1.64)

II. ☐ Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)

- i. A request for continued examination has been filed with, or prior to, this form.
- ii. If the application is a utility application, this certification and request is being filed via EFS-Web.
- iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
- iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
- v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

Signature 	Date April 17, 2014
Name (Print/Typed) Lawrence F. Rozsnyai	Practitioner Registration Number 58,427
Note: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.*	
☒ *Total of <u>1</u> forms are submitted.	

Document code: WFEE

United States Patent and Trademark Office
Sales Receipt for Accounting Date: 05/06/2014

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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 14/255,833		Filing Date 04/17/2014		☐ To be Mailed	
ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO									
APPLICATION AS FILED – PART I									
(Column 1)		(Column 2)							
FOR	NUMBER FILED	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), (l), 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									
(Column 1)		(Column 2)		(Column 3)					
AMENDMENT	07/07/2014	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(i))	* 11	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	
(Column 1)		(Column 2)		(Column 3)					
AMENDMENT	04/17/2014	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(i))	* 11	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.									

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.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875						Application or Docket Number 14/255,833		
APPLICATION AS FILED - PART I <div style="display: flex; justify-content: space-around; font-size: small;"> (Column 1) (Column 2) </div>								
FOR	NUMBER FILED	NUMBER EXTRA	SMALL ENTITY	OR	OTHER THAN SMALL ENTITY			
BASIC FEE <small>(37 CFR 1.16(a), (b), or (c))</small>	N/A	N/A	RATE(\$)		RATE(\$)		FEE(\$)	
SEARCH FEE <small>(37 CFR 1.16(k), (l), or (m))</small>	N/A	N/A	N/A		N/A		280	
EXAMINATION FEE <small>(37 CFR 1.16(o), (p), or (q))</small>	N/A	N/A	N/A		N/A		600	
TOTAL CLAIMS <small>(37 CFR 1.16(i))</small>	11	minus 20 = *			x 80 =		0.00	
INDEPENDENT CLAIMS <small>(37 CFR 1.16(h))</small>	1	minus 3 = *			x 420 =		0.00	
APPLICATION SIZE FEE <small>(37 CFR 1.16(s))</small>	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 <div style="display: flex; justify-content: space-around; font-size: x-small;"> (Column 1) (Column 2) (Column 3) </div>								
AMENDMENT A		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	SMALL ENTITY	OR	OTHER THAN SMALL ENTITY
	Total <small>(37 CFR 1.16(i))</small>	*	Minus	**	=	RATE(\$)		RATE(\$)
	Independent <small>(37 CFR 1.16(h))</small>	*	Minus	***	=	ADDITIONAL FEE(\$)		ADDITIONAL FEE(\$)
	Application Size Fee (37 CFR 1.16(s))							
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
						TOTAL ADD'L FEE		TOTAL ADD'L FEE
AMENDMENT B		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	SMALL ENTITY	OR	OTHER THAN SMALL ENTITY
	Total <small>(37 CFR 1.16(i))</small>	*	Minus	**	=	RATE(\$)		RATE(\$)
	Independent <small>(37 CFR 1.16(h))</small>	*	Minus	***	=	ADDITIONAL FEE(\$)		ADDITIONAL FEE(\$)
	Application Size Fee (37 CFR 1.16(s))							
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
						TOTAL ADD'L FEE		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.								



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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
14/255,833	04/17/2014	1673	5600	PH3080.PC7-TRK1	11	1

CONFIRMATION NO. 5585

25000
GILEAD SCIENCES, INC
333 LAKESIDE DR
FOSTER CITY, CA 94404

FILING RECEIPT



Date Mailed: 05/07/2014

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, Foster City, CA;

Applicant(s)

Gilead Pharmasset LLC, Foster City, CA

Assignment For Published Patent Application

Gilead Pharmasset LLC, Foster City, CA

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 14/057,675 10/18/2013
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.

If Required, Foreign Filing License Granted: 05/06/2014

page 1 of 3

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 14/255,833**

Projected Publication Date: To Be Determined - pending completion of Sequence Disclosures

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



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/255,833	04/17/2014	Jinfa Du	PH13080.PC7-TRK1

CONFIRMATION NO. 5585

FORMALITIES LETTER

25000
GILEAD SCIENCES, INC
333 LAKESIDE DR
FOSTER CITY, CA 94404



Date Mailed: 05/07/2014

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT
APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE
AND/OR AMINO ACID SEQUENCE DISCLOSURES**

Filing Date Granted

Applicant is given **TWO MONTHS FROM THE DATE OF THIS NOTICE** within which to comply with the sequence rules, 37 CFR §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR § 1.821(g). Extension of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR § 1.136.

- 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, 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.

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.

For questions regarding compliance to these requirements, please contact:

- For Rules interpretation, call (571) 270-5300
- For CRF submission help, call (571) 272-2510
- For PatentIn software program support technical assistance, call (866)217-9197.

page 1 of 2

- 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> .

Items Required To Avoid Processing Delays:

Applicant is notified that the above-identified application contains the deficiencies noted below. No period for reply is set forth in this notice for correction of these deficiencies. However, if a deficiency relates to the inventor's oath or declaration, the applicant must file an oath or declaration in compliance with 37 CFR 1.63, or a substitute statement in compliance with 37 CFR 1.64, executed by or with respect to each actual inventor no later than the expiration of the time period set in the "Notice of Allowability" to avoid abandonment. See 37 CFR 1.53(f).

A new inventor's oath or declaration that identifies this application (e.g., by Application Number and filing date) is required. The inventor's oath or declaration does not comply with 37 CFR 1.63 in that it:

- does not state that the above-identified application was made or authorized to be made by the person executing the oath or declaration.

Jinfa Du

Dhanapalan Nagarathnam

Michael Joseph Sofia

Peiyuan Wang

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.

/tnghuyen/

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



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/255,833	04/17/2014	Jinfa Du	PH13080.PC7-TRK1

25000
GILEAD SCIENCES, INC
333 LAKESIDE DR
FOSTER CITY, CA 94404

CONFIRMATION NO. 5585
IMPROPER CPOA LETTER



Date Mailed: 05/07/2014

NOTICE REGARDING POWER OF ATTORNEY

This is in response to the power of attorney filed 04/17/2014. The power of attorney in this application is not accepted for the reason(s) listed below:

- The power of attorney has not been accepted because the party who is giving power has not been identified. Power of attorney may only be signed by the applicant for patent (37 CFR 1.42) or the patent owner. A party who is not the applicant must become the applicant in accordance with 37 CFR 1.46(c) and appoint any power of attorney in compliance with 37 CFR 3.71 and 3.73. For a reissue application, reexamination proceeding, or supplemental examination proceeding, a patent owner who was not the applicant under 37 CFR 1.46 must appoint any power of attorney in compliance with 37 CFR 3.71 and 3.73. See 37 CFR 1.32(b)(4).

/tha/

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): Jinfa Du, et al.
Title: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
Appl. No. 14/255,833
Filing Date 04/17/2014
Examiner: Not Yet Assigned
Art Unit: 1673
Confirmation No.: 5585

**TRANSMITTAL OF NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT
APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID
SEQUENCE DISCLOSURES**

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

Commissioner:

In response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures mailed May 7, 2014 in the above-identified patent application, transmitted herewith are the items to complete the filing of the subject patent application. The Notice provided two-months to respond. This Response is timely filed on July 7, 2014.

Enclosed are:

- [X] Copy of Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures (2 pages)
- [X] Statement to Support Filing and Submission in Accordance with 37 C.F.R. §§1.821-1.825 (1 page)
- [X] Amendment in Response to Notice under 37 C.F.R. §§1.821-1.825 (3 pages)
- [X] Sequence Listing in ASCII format (2 pages)

- ☒ Sequence Listing in PDF format (2 pages)
- ☒ Declarations (37 C.F.R. 1.63) for Utility Application (4 pages)

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. 50-6219. If any 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. 50-6219.

Respectfully submitted,

Date July 7, 2014

By /Neeta C. Thakur/

Sheppard, Mullin, Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301
Telephone: (650) 815-2600

Neeta C. Thakur, Ph.D.
Agent for Applicant
Registration No. 59,123



UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/255,833	04/17/2014	Jinfa Du	PH13080.PC7-TRK1

CONFIRMATION NO. 5585

FORMALITIES LETTER

25000
GILEAD SCIENCES, INC
333 LAKESIDE DR
FOSTER CITY, CA 94404



Date Mailed: 05/07/2014

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT
APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE
AND/OR AMINO ACID SEQUENCE DISCLOSURES**

Filing Date Granted

Applicant is given **TWO MONTHS FROM THE DATE OF THIS NOTICE** within which to comply with the sequence rules, 37 CFR §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR § 1.821(g). Extension of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR § 1.136.

- 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, 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.

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.

For questions regarding compliance to these requirements, please contact:

- For Rules interpretation, call (571) 270-5300
- For CRF submission help, call (571) 272-2510
- For PatentIn software program support technical assistance, call (866)217-9197.

page 1 of 2

- 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> .

Items Required To Avoid Processing Delays:

Applicant is notified that the above-identified application contains the deficiencies noted below. No period for reply is set forth in this notice for correction of these deficiencies. However, if a deficiency relates to the inventor's oath or declaration, the applicant must file an oath or declaration in compliance with 37 CFR 1.63, or a substitute statement in compliance with 37 CFR 1.64, executed by or with respect to each actual inventor no later than the expiration of the time period set in the "Notice of Allowability" to avoid abandonment. See 37 CFR 1.53(f).

A new inventor's oath or declaration that identifies this application (e.g., by Application Number and filing date) is required. The inventor's oath or declaration does not comply with 37 CFR 1.63 in that it:

- does not state that the above-identified application was made or authorized to be made by the person executing the oath or declaration.

Jinfa Du

Dhanapalan Nagarathnam

Michael Joseph Sofia

Peiyuan Wang

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:

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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.

/tnghuyen/

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No: PH3080.PC7-TRK1

In re patent application of
DU, JINFA et al.
Serial No.: 14/255,833
Filed: April 17, 2014
For: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

STATEMENT TO SUPPORT FILING AND SUBMISSION IN
ACCORDANCE WITH 37 C.F.R. §§1.821-1.825

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Mail Stop SEQUENCE

Sir:

In connection with the Sequence Listing submitted concurrently herewith, the undersigned hereby states that:

1. the content of the electronically filed submission is in accordance with 37 C.F.R. §1.821(e); and
2. the submission, in accordance with 37 C.F.R. §1.821(g), does not include new matter.

Respectfully submitted,

July 7, 2014
Date

/tara rix/
Tara Rix

HARBOR CONSULTING IP SERVICES, INC.
1039 Islington Street, Suite 13
Portsmouth, NH 03801
800-318-3021

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): Jinfu Du, et al.
Title: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
Appl. No. 14/255,833
Filing Date 04/17/2014
Examiner: Not Yet Assigned
Art Unit: 1673
Confirmation No.: 5585

AMENDMENT IN RESPONSE TO NOTICE UNDER 37 CFR §§1.821-825

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

Commissioner:

In response to the Notice to Comply mailed May 7, 2014, please amend the application as follows:

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. Said ASCII copy, created on July 7, 2014, is named PH3080.PC7-TRK1_SL.txt and is 1,253 bytes in size.

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

REMARKS

The foregoing amendments are made to insert the required SEQ ID NO identifiers associated with each listed sequence, as well as to incorporate by reference the Sequence Listing filed concurrently herewith.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

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. 50-6219. If any 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. 50-6219.

Respectfully submitted,

Date July 7, 2014

By /Neeta C. Thakur/

Sheppard, Mullin, Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301
Telephone: (650) 815-2600

Neeta C. Thakur, Ph.D.
Agent for Applicant
Registration No. 59,123

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN
APPLICATION DATA SHEET (37 CFR 1.76)Title of
Invention

NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

As the below named inventor, I hereby declare that:

This declaration ☐ The attached application, or
is directed to:☒ United States application or PCT international application number 14/255,833
filed on April 17, 2014

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001
by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identify them. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioner/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Michael J. SofiaDate (Optional): 6/10/2014Signature: Michael J. Sofia

Note: An application data sheet (PTO/SF/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

**DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN
APPLICATION DATA SHEET (37 CFR 1.76)**

Title of
Invention

NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

As the below named inventor, I hereby declare that:

This declaration
is directed to:

☐

The attached application, or

☒

United States application or PCT international application number 14/255,833

filed on April 17, 2014

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001
by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Peiyuan Wang

Date (Optional): June 9, 2014

Signature:

Peiyuan Wang

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

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.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN
APPLICATION DATA SHEET (37 CFR 1.76)Title of
invention

NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

As the below named inventor, I hereby declare that:

This declaration
is directed to:

The attached application, or



United States application or PCT international application number

14/255,893

filed on April 17, 2014

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001
by fine or imprisonment of not more than five (5) years, or both.

WARNING:

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LEGAL NAME OF INVENTOR

Inventor: Dhanapalan Nagarathnam

Date (Optional):

Signature:

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

PH0880/PC7-TK0
350938.1

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.

**DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN
APPLICATION DATA SHEET (37 CFR 1.76)****Title of
Invention**

NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

As the below named inventor, I hereby declare that:

This declaration ☐ The attached application, or
is directed to:☒ United States application or PCT international application number 14/265,833
filed on April 17, 2014

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001
by fine or imprisonment of not more than five (5) years, or both.**WARNING:**

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTORInventor: Jinfu DuDate (Optional): 6/12/2014Signature: 

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/D1 form for each additional inventor.

PH3080_PC7-TRK1_SL.txt
SEQUENCE LISTING

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

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Electronic Acknowledgement Receipt	
EFS ID:	19510890
Application Number:	14255833
International Application Number:	
Confirmation Number:	5585
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	25000
Filer:	Neeta C. Thakur/Rachel Mena
Filer Authorized By:	Neeta C. Thakur
Attorney Docket Number:	PH3080.PC7-TRK1
Receipt Date:	07-JUL-2014
Filing Date:	17-APR-2014
Time Stamp:	20:20:25
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Applicant Response to Pre-Exam Formalities Notice	37JD_199059_US6_Response_to_Notice_to_Comply.pdf	86207 61ac0219d26e57a0d74d0fe1da88b63fa4c929c	no	2

Warnings:

Information:

2	Applicant Response to Pre-Exam Formalities Notice	37JD_199059_US6_Notice_to_Comply.pdf	115624	no	2
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Warnings:					
Information:					
3	CRF Statement Paper and CRF are the same	37JD_199059_US6_Statement.pdf	68527	no	1
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	Preliminary Amendment		1	1	
	Specification		2	2	
	Applicant Arguments/Remarks Made in an Amendment		3	3	
Warnings:					
Information:					
5	Oath or Declaration filed	37JD_199059_US6_Declarations.pdf	747515	no	4
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Warnings:					
Information:					
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Information:					
Total Files Size (in bytes):			1132451		

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.

SCORE Placeholder Sheet for IFW Content

Application Number: 14255833

Document Date: 07/07/2014

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.

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Sequence Listing was accepted.

If you need help call the Patent Electronic Business Center at (866)
217-9197 (toll free).

Reviewer: Saleem, Syed (ASRC)

Timestamp: [year=2014; month=7; day=8; hr=10; min=35; sec=27; ms=806;]

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Validated By CRFValidator v 1.0.4

Application No: 14255833 Version No: 1.0

Input Set:

Output Set:

Started: 2014-07-07 20:20:27.952
Finished: 2014-07-07 20:20:28.092
Elapsed: 0 hr(s) 0 min(s) 0 sec(s) 140 ms
Total Warnings: 3
Total Errors: 0
No. of SeqIDs Defined: 3
Actual SeqID Count: 3

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SEQUENCE LISTING

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SOFIA, MICHAEL JOSEPH
WANG, PEIYUAN

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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875						Application or Docket Number 14/255,833				
APPLICATION AS FILED - PART I										
(Column 1)		(Column 2)		SMALL ENTITY		OTHER THAN SMALL ENTITY				
FOR	NUMBER FILED	NUMBER EXTRA	RATE(\$)	FEE(\$)		RATE(\$)	FEE(\$)			
BASIC FEE <small>(37 CFR 1.16(a), (b), or (c))</small>	N/A	N/A	N/A			N/A	280			
SEARCH FEE <small>(37 CFR 1.16(k), (l), or (m))</small>	N/A	N/A	N/A			N/A	600			
EXAMINATION FEE <small>(37 CFR 1.16(o), (p), or (q))</small>	N/A	N/A	N/A			N/A	720			
TOTAL CLAIMS <small>(37 CFR 1.16(i))</small>	11	minus 20 = *			OR	x 80 =	0.00			
INDEPENDENT CLAIMS <small>(37 CFR 1.16(h))</small>	1	minus 3 = *				x 420 =	0.00			
APPLICATION SIZE FEE <small>(37 CFR 1.16(s))</small>	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)		(Column 2)		(Column 3)		SMALL ENTITY		OTHER THAN SMALL ENTITY		
AMENDMENT A		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)
	Total <small>(37 CFR 1.16(i))</small>	*	Minus	**	=	x	=	OR	x	=
	Independent <small>(37 CFR 1.16(h))</small>	*	Minus	***	=	x	=	OR	x	=
	Application Size Fee (37 CFR 1.16(s))							OR		
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE			OR	TOTAL ADD'L FEE	
AMENDMENT B		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)
	Total <small>(37 CFR 1.16(i))</small>	*	Minus	**	=	x	=	OR	x	=
	Independent <small>(37 CFR 1.16(h))</small>	*	Minus	***	=	x	=	OR	x	=
	Application Size Fee (37 CFR 1.16(s))							OR		
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE			OR	TOTAL ADD'L FEE	
<div style="font-size: x-small;"> * 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. </div>										



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UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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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
14/255,833	04/17/2014	1673	5600	37JD-199059-US6	11	1

CONFIRMATION NO. 5585

UPDATED FILING RECEIPT



25000
GILEAD SCIENCES, INC
333 LAKESIDE DR
FOSTER CITY, CA 94404

Date Mailed: 07/15/2014

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, Foster City, CA;

Applicant(s)

Gilead Pharmasset LLC, Foster City, CA

Assignment For Published Patent Application

Gilead Pharmasset LLC, Foster City, CA

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 14/057,675 10/18/2013 PAT 8735372
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.

If Required, Foreign Filing License Granted: 05/06/2014

page 1 of 3

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 14/255,833**

Projected Publication Date: 10/23/2014

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 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 Assets Control, 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

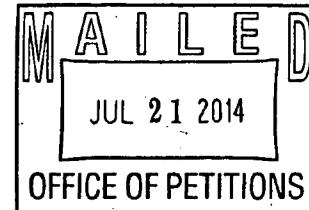
The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through 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 technology, manufacture products, deliver services, and grow your business, visit <http://www.SelectUSA.gov> or call +1-202-482-6800.



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333 LAKESIDE DR
FOSTER CITY CA 94404



Doc Code: TRACK1.GRANT

Decision Granting Request for Prioritized Examination (Track I or After RCE)	Application No.: 14/255,833
<p>1. THE REQUEST FILED <u>April 17, 2014</u> IS GRANTED.</p> <p>The above-identified application has met the requirements for prioritized examination</p> <p>A. ☒ for an original nonprovisional application (Track I). B. ☐ for an application undergoing continued examination (RCE).</p> <p>2. The above-identified application will undergo prioritized examination. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:</p> <p>A. filing a <u>petition for extension of time</u> to extend the time period for filing a reply; B. filing an <u>amendment to amend the application to contain more than four independent claims, more than thirty total claims</u>, or a multiple dependent claim; C. filing a <u>request for continued examination</u>; D. filing a notice of appeal; E. filing a request for suspension of action; F. mailing of a notice of allowance; G. mailing of a final Office action; H. completion of examination as defined in 37 CFR 41.102; or I. abandonment of the application.</p> <p>Telephone inquiries with regard to this decision should be directed to <u>Michelle R. Eason</u> at (571) 272-4231. In his/her absence, calls may be directed to Brian W. Brown at (571) 272-5338.</p> <p><u>/Michelle R. Eason/</u> (Signature)</p> <p><u>Paralegal Specialist, Office of Petitions</u> (Title)</p>	

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

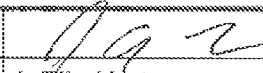
☐	Firm or Individual Name			
	Address			
	City	State	Zip	
	Country			
	Telephone	Email		

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 Hartum	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.

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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.

STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: GILEAD PHARMASSET LLC
Application No./Patent No.: 14/255,833 Filed/Issue Date: April 17, 2014
Titled: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
GILEAD PHARMASSET LLC, a CORPORATION
(Name of Assignee) (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. ☒ 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. ☒ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: DU ET AL. To: PHARMASSET, INC.

The document was recorded in the United States Patent and Trademark Office at
Reel 033404, Frame 0944, or for which a copy thereof is attached.

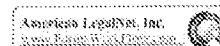
2. From: PHARMASSET, INC. To: GILEAD PHARMASSET LLC

The document was recorded in the United States Patent and Trademark Office at
Reel 033429, Frame 0375, or for which a copy thereof is attached.

[Page 1 of 2]

This collection of information is required by 37 CFR 3.73(b). 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 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.

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STATEMENT UNDER 37 CFR 3.73(c)

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Reel _____, Frame _____, or for which a copy thereof is attached.

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The document was recorded in the United States Patent and Trademark Office at
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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.

NThakur (Reg.No. 59,123)

Aug. 22, 2014

Signature

Date

for
Lorna L. Tanner

50782

Printed or Typed Name

Title or Registration Number

[Page 2 of 2]

Electronic Acknowledgement Receipt	
EFS ID:	19945301
Application Number:	14255833
International Application Number:	
Confirmation Number:	5585
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	25000
Filer:	Lorna Lea Tanner/christa carter
Filer Authorized By:	Lorna Lea Tanner
Attorney Docket Number:	37JD-199059-US6
Receipt Date:	22-AUG-2014
Filing Date:	17-APR-2014
Time Stamp:	17:26:41
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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Warnings:

The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing

Information:

2	Assignee showing of ownership per 37 CFR 3.73.	14255833.pdf	421429	no	2
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Warnings:

Information:

Total Files Size (in bytes):		612476
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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.

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Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: August 25, 2014 <i>(use as many sheets as necessary)</i>				Application Number	14/255,833
				Filing Date	04/17/2014
				First Named Inventor	Jinfa Du
				Art Unit	1673
				Examiner Name	LEWIS, PATRICK T
Sheet	1	of	3	Attorney Docket Number	37JD-199059-US7

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
		20050059632	03-17-2005	Storer, et al.	
		20130109647	05-02-2013	Berrey ((PH50X2.P2C, 37JD-197437-US)	
		20130136776	05-30-2013	Cleary (PH50X3.PC, 37JD-197436-US)	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	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
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				

Examiner Signature		Date Considered	
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP . if possible. and . 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 . This collection is estimated to take 2 hours 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, 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 (1-800-786-9199) and select option 2.

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Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: August 25, 2014 <i>(use as many sheets as necessary)</i>		Application Number	14/255,833
		Filing Date	04/17/2014
		First Named Inventor	Jinfa Du
		Art Unit	1673
		Examiner Name	LEWIS, PATRICK T
Sheet 2 of 3	Attorney Docket Number	37JD-199059-US7	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
		Codington, et al., "Nucleosides. XVIII. Synthesis of 2'-Fluorothymidine, 2'-Fluorodeoxyuridine, and Other 2'-Halogeno-2'-Deoxy Nucleosides ^{1,2n} , The Division of Nucleoprotein Chemistry, Sloan-Kettering Institute for Cancer Research, Sloan-Kettering Division of Cornell University Medical Colleg, New York 21, New York, Vol. 29, pages 558-564, (1963).	
		Hrebabecky, et al., "1-(3,5- <i>O</i> -alkylidene-2-deoxy-4-C-hydroxymethyl- α -L- <i>threo</i> -pentofuranosyl)uracils," Collect. Czech. Chem. Commun., Vol. 62, pages 957-970, (1997).	
		Hrebabecky, et al., "Synthesis of 1-(3-azido-2,3-dideoxy- β -D-allofuranosyl)thymine, 1-(2,3-dideoxy- β -D-allofuranosyl)thymine, and 1-(2,3-dideoxy- β -D- <i>erythro</i> -hex-2-enofuranosyl)thymine," Carbohydrate Research, Vol. 216, pages 179-186, (1991).	
		Hrebabecky, et al., "Synthesis of 1-(3-azido-2,3-dideoxy- β -d- <i>ribo</i> -hexofuranosyl)-, 1-(2,3-dideoxy- β -d- <i>erythro</i> -hexofuranosyl)- and 1-(2,3-dideoxy- β -d- <i>erythro</i> -hex-2-enofuranosyl)pyrimidine nucleosides," Collect. Czech. Chem. Commun., Vol. 59, pages 412-420, (1993).	
		Hrebabecky, et al., "Synthesis of 1-(3-azido-2,3-dideoxy-4-C-hydroxymethyl- α -L- <i>threo</i> -pentofuranosyl)thymine, 1-(2,3-dideoxy-4-C-hydroxy-methyl- α -L- <i>glycero</i> -pentofuranosyl)thymine and 1-(2,3-dideoxy-4-C-hydroxymethyl- α -L- <i>glycero</i> -pent-2-enofuranosyl)thymine," Collect Czech. Chem. Commun., Vol. 58, pages 409-420, (1992).	
		Lin, et al., "A stereospecific synthesis of 2',3'-dideoxy- β -L-cytidine (β -L-ddC), a potent inhibitor against human hepatitis B virus (HBV) and human immunodeficiency virus (HIV)," Tetrahedron Letters, Vol. 35, No. 21, pages 3477-3480, (1994).	
		Mourier, et al., "Enantioselective synthesis and biological evaluation of 5- <i>o</i> -carboranyl-pyrimidine-nucleosides," Bioorganic & Medicinal Chemistry, Vol 7, pages 2759-2766, (1999).	
		Robins, et al., "Nucleic acid related compounds. 91. Biomimetic reactions are in harmony with loss of 2'-substituents as free radicals (not anions) during mechanism-based inactivation of ribonucleotide reductases. differential interactions of azide, halogen, and alkylthio groups with tributylstannane and triphenylsilane," Journal of the American Chemical Society, Vol. 118, No. 46, pages 11341-11348, (1996).	
		Saneyoshi, "Facile synthesis of 2'- <i>O</i> -cyanoethyluridine by ring-opening reaction of 2,2'-anhydrouridine with cyanoethyl trimethylsilyl ether in the presence of BF ₃ Et ₂ O," Tetrahedron Letters, Vol. 48, pages 8554-8557, (2007).	
		Van Rompaey, et al., "Mycobacterium tuberculosis thymidine monophosphate kinase inhibitors; biological evaluation and conformational analysis of 2'-and 3'-modified thymidine analogues," Eur. J. Org. Chem., pages 2911-2918, (2003).	

Examiner Signature	Date Considered
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP . if possible. and . 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 . This collection is estimated to take 2 hours 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, 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.**

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Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: August 25, 2014 <i>(use as many sheets as necessary)</i>		Application Number	14/255,833
		Filing Date	04/17/2014
		First Named Inventor	Jinfa Du
		Art Unit	1673
		Examiner Name	LEWIS, PATRICK T
Sheet 3 of 3	Attorney Docket Number	37JD-199059-US7	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
		Vanheusden, et al., "Synthesis and evaluation of thymidine-5'-O-monophosphate analogues as inhibitors of <i>mycobacterium tuberculosis</i> thymidylate kinase," Bioorganic & Medicinal Chemistry Letters, Vol. 12, pages 2695-2698, (2002).	
		Vanheusden, et al., "Discovery of bicyclic thymidine analogues as selective and high-affinity inhibitors of <i>mycobacterium tuberculosis</i> thymidine monophosphate kinase," J. Med. Chem., Vol. 47, pages 6187-6194, (2004).	

SMRH:430949874.1

Examiner Signature	Date Considered
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP . if possible. and . 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 . This collection is estimated to take 2 hours 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, 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.**

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Electronic Acknowledgement Receipt	
EFS ID:	19957304
Application Number:	14255833
International Application Number:	
Confirmation Number:	5585
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Jinfa Du
Customer Number:	25000
Filer:	Neeta C. Thakur/Rachel Mena
Filer Authorized By:	Neeta C. Thakur
Attorney Docket Number:	37JD-199059-US6
Receipt Date:	25-AUG-2014
Filing Date:	17-APR-2014
Time Stamp:	21:22:33
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Non Patent Literature	Codington_1963.pdf	2674133	no	7
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Warnings:

Information:

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Information:					
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Warnings:					
Information:					
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Warnings:					
Information:					
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Warnings:					
Information:					
6	Non Patent Literature	Lin_Tet_Lett_1994.pdf	616789	no	4
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Warnings:					
Information:					
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Information:					

11	Non Patent Literature	Vanheusden_Bioorg_Med_Chem_Lett_2002.pdf	141505 ad30e9c7e8bd53036bfff748fae1c5f89cc18ef1a	no	4
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Information:					
13	Transmittal Letter	37JD_199059_US7_IDS_Transmittal.pdf	86019 8a77ca002d57241e18e4cff60d0fe07d0cd31dae0	no	2
Warnings:					
Information:					
14	Information Disclosure Statement (IDS) Form (SB08)	37JD_199059_US7_IDS_SB08.pdf	138259 3d93337c5a7ac0b76354e9b9782c7bfff26808bc	no	3
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
Total Files Size (in bytes):			9924257		
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): Jinfa Du, et al.
Title: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
Appl. No. 14/255,833
Filing Date 04/17/2014
Examiner: LEWIS, PATRICK T
Art Unit: 1673
Confirmation No.: 5585

INFORMATION DISCLOSURE STATEMENT
UNDER 37 C.F.R. §1.56

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

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 C.F.R. §§1.56, 1.97 and 1.98.

Applicants respectfully request that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with M.P.E.P. §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 C.F.R. §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

SMRH:431130694.1

-1-

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 C.F.R. §1.97(b), before the mailing date of the first Office Action on the merits.

Although Applicants believe that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 50-6219.

Respectfully submitted,

Date August 25, 2014

By /Neeta C. Thakur/

Sheppard, Mullin, Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301
Telephone: (650) 815-2600

Neeta C. Thakur, Ph.D.
Agent for Applicant
Registration No. 59,123



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
14/255,833	04/17/2014	Jinfa Du	37JD-199059-US6

CONFIRMATION NO. 5585
POA ACCEPTANCE LETTER

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



Date Mailed: 09/02/2014

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 08/22/2014.

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.

/qtran/

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



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
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NOTICE OF ALLOWANCE AND FEE(S) DUE

117796 7590 09/10/2014
Gilad Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301

EXAMINER

LEWIS, PATRICK T

ART UNIT

PAPER NUMBER

1672

DATE MAILED: 09/10/2014

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/255,833	04/17/2014	Jinfa Du	37JD-199059-US6	5585

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
nonprovisional	UNDISCOUNTED	\$960	\$0	\$0	\$960	12/10/2014

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.

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 09/10/2014
Gilead Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301

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.
14/255,833	04/17/2014	Jinfa Du	37JD-199059-US6	5585

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
nonprovisional	UNDISCOUNTED	\$960	\$0	\$0	\$960	12/10/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
LEWIS, PATRICK T	1672	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. _____



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 NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/255,833	04/17/2014	Jinfa Du	37JD-199059-US6	5585

117796 7590 09/10/2014
Gilad Sciences, Inc.
c/o Sheppard Mullin Richter & Hampton LLP
379 Lytton Avenue
Palo Alto, CA 94301

EXAMINER

LEWIS, PATRICK T

ART UNIT	PAPER NUMBER
----------	--------------

1672

DATE MAILED: 09/10/2014

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

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. 14/255,833	Applicant(s) DU ET AL.	
	Examiner PATRICK LEWIS	Art Unit 1672	AI/A (First Inventor to File) 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 _____.
☐ 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 4-14. 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 a reply 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)	5. ☒ Examiner's Amendment/Comment
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date <u>04172014; 08252014</u>	6. ☒ Examiner's Statement of Reasons for Allowance
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material	7. ☐ Other _____.
4. ☒ Interview Summary (PTO-413), Paper No./Mail Date <u>20140825</u> .	

/PATRICK LEWIS/ Primary Examiner, Art Unit 1672	
--	--

DETAILED ACTION

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.

Authorization for this examiner's amendment was given in a telephone interview with Dr. Neeta Thakur on August 22, 2014.

The application has been amended as follows:

In claim 4, line 11, after the semicolon “;”, the term ---and--- has been inserted.

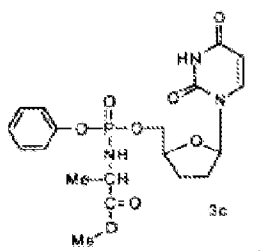
In claim 10, line 2, the term “claim 1” has been deleted and the term ---claim 4--- has been inserted therefor.

In claim 11, line 1, before the term “subject”, the term ---human--- has been inserted.

In claim 14, line 1, before the term “subject”, the term ---human--- has been inserted.

Allowable Subject Matter

3. The following is an examiner's statement of reasons for allowance: McGuigan et al. FEBS Letters (1994), Vol. 351, pages 11-14 (McGuigan) is representative of prior art. McGuigan teaches



The prior art does not teach nor suggest the instantly claimed compound.

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."

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PATRICK LEWIS whose telephone number is (571)272-0655. The examiner can normally be reached on Monday - Thursday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. 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 LEWIS/
Primary Examiner, Art Unit 1672

/PL/

Notice of References Cited	Application/Control No. 14/255,833	Applicant(s)/Patent Under Reexamination DU ET AL.	
	Examiner PATRICK LEWIS	Art Unit 1672	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

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

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	McGuigan et al. FEBS Letters (1994), Vol. 351, pages 11-14.
	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.

(FILE 'HOME' ENTERED AT 13:52:23 ON 19 AUG 2014)

FILE 'REGISTRY' ENTERED AT 13:52:34 ON 19 AUG 2014

L1	STRUCTURE UPLOADED
L2	0 S L1 SSS SAM
L3	0 S L1 SSS FULL

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: 4/17/2014 Signature: L.F. Rozsnyai
(Lawrence F. Rozsnyai)

Docket No.: PH3080.PC7-TRK1
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Jinfa Du et al.

Application No.: Not Yet Assigned

Confirmation No.: N/A

Filed: Concurrently Herewith

Art Unit: N/A

For: NUCLEOSIDE PHOSPHORAMIDATE
PRODRUGS

Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

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

Dear Madam:

Pursuant to 37 C.F.R. § 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement accompanies the new patent application submitted herewith.

Copies of the references on the PTO/SB/08 are not supplied because they were previously cited by or submitted to the Office in prior application numbers 14/057,675 filed October 18, 2013 and 13/609,614 filed September 11, 2012 relied upon in these applications for an earlier filing date under 35 U.S.C. § 120.

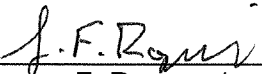
In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. § 1.56(a) exists. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98 and the Examiner is respectfully requested to consider the listed references.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 07-1250, under Order No. PH3080.PC7-TRK1.

Dated: April 17, 2014

Respectfully submitted,

By 

Lawrence F. Rozsnyai

Registration No.: 58,427

GILEAD SCIENCES, INC.

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Attorney For Applicant

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number		13609614
	Filing Date		2012-09-11
	First Named Inventor	Michael Joseph Sofia	
	Art Unit	1623	
	Examiner Name	Patrick T. Lewis	
	Attorney Docket Number	03956.053800.2	

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