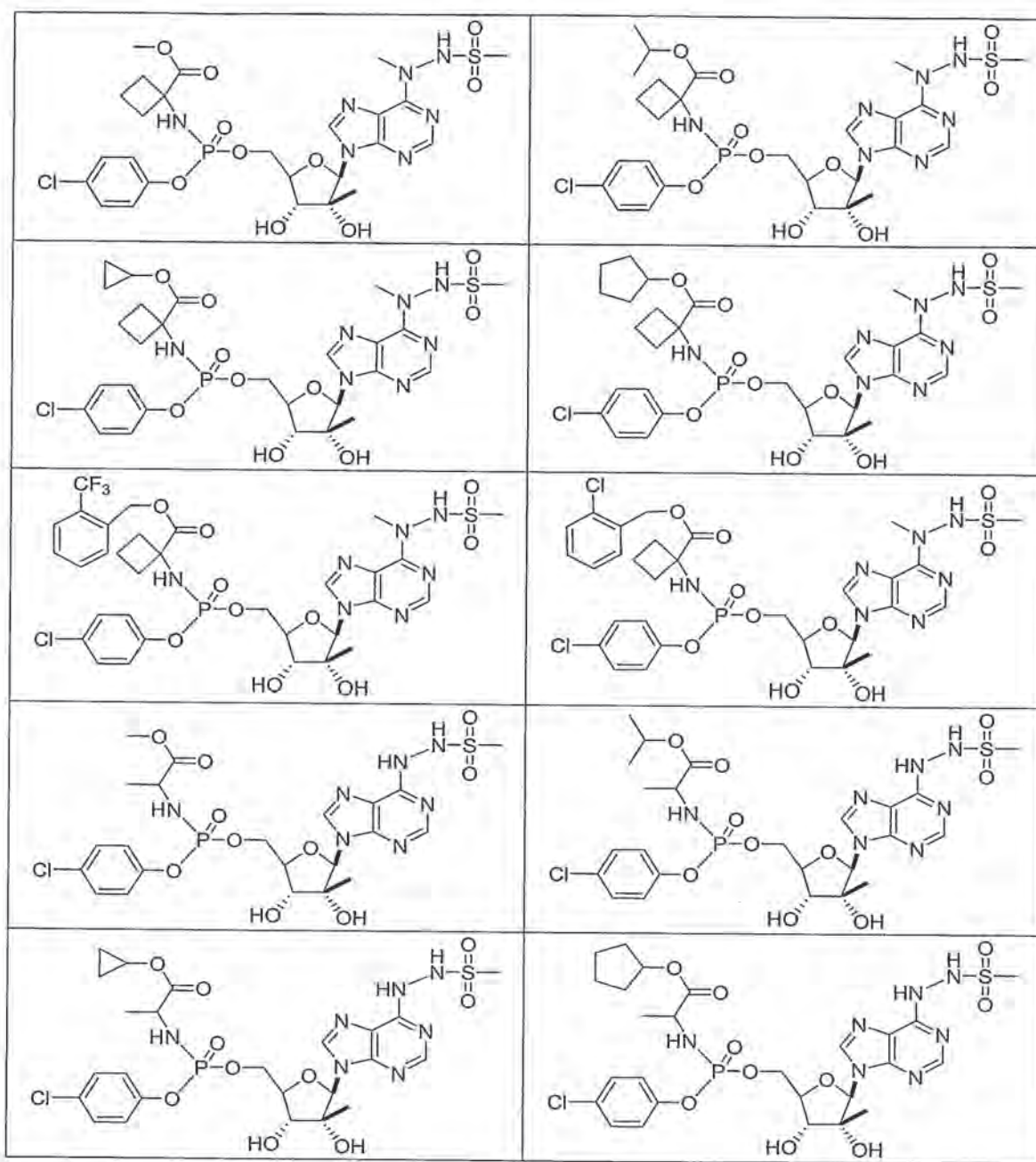
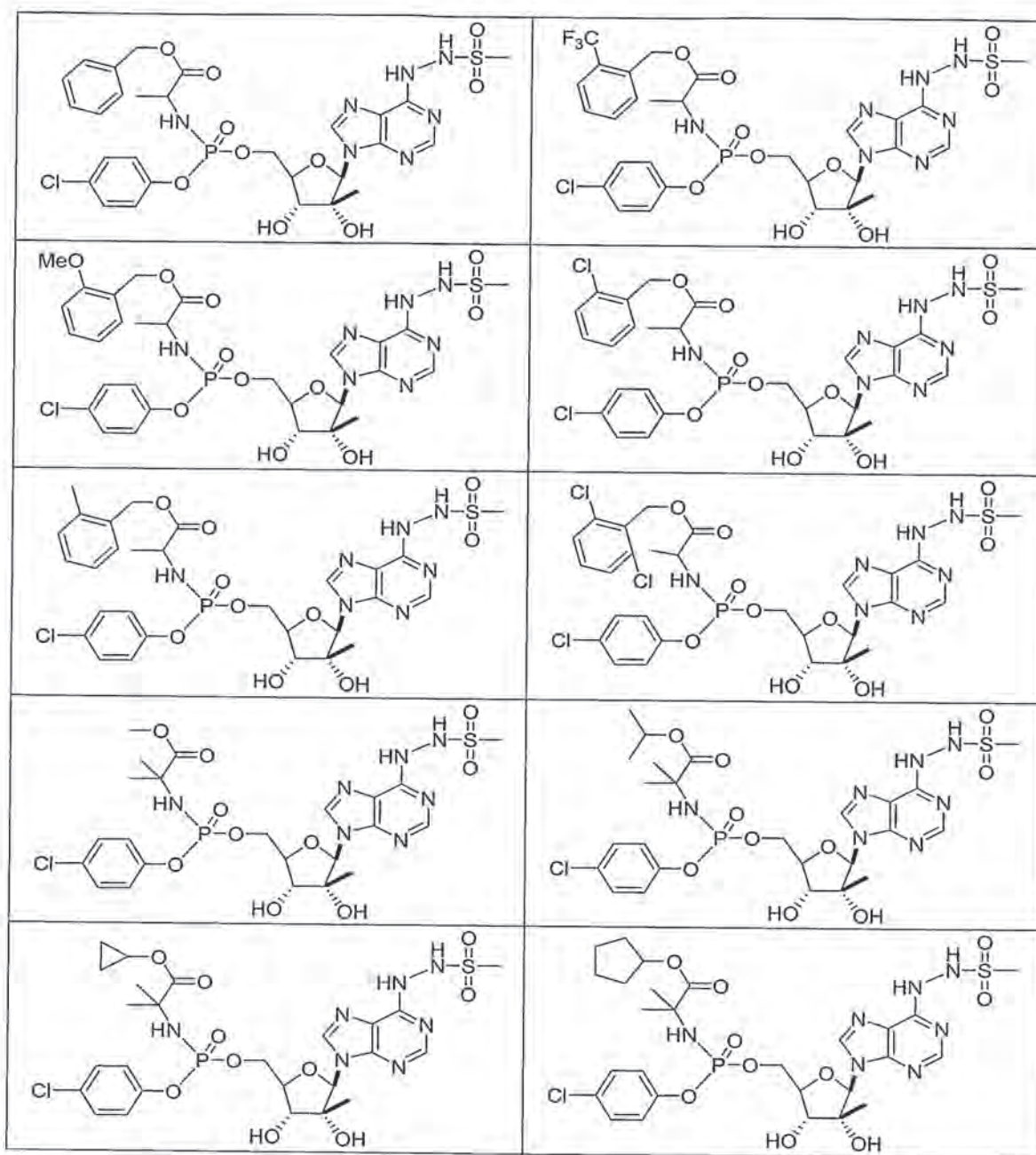
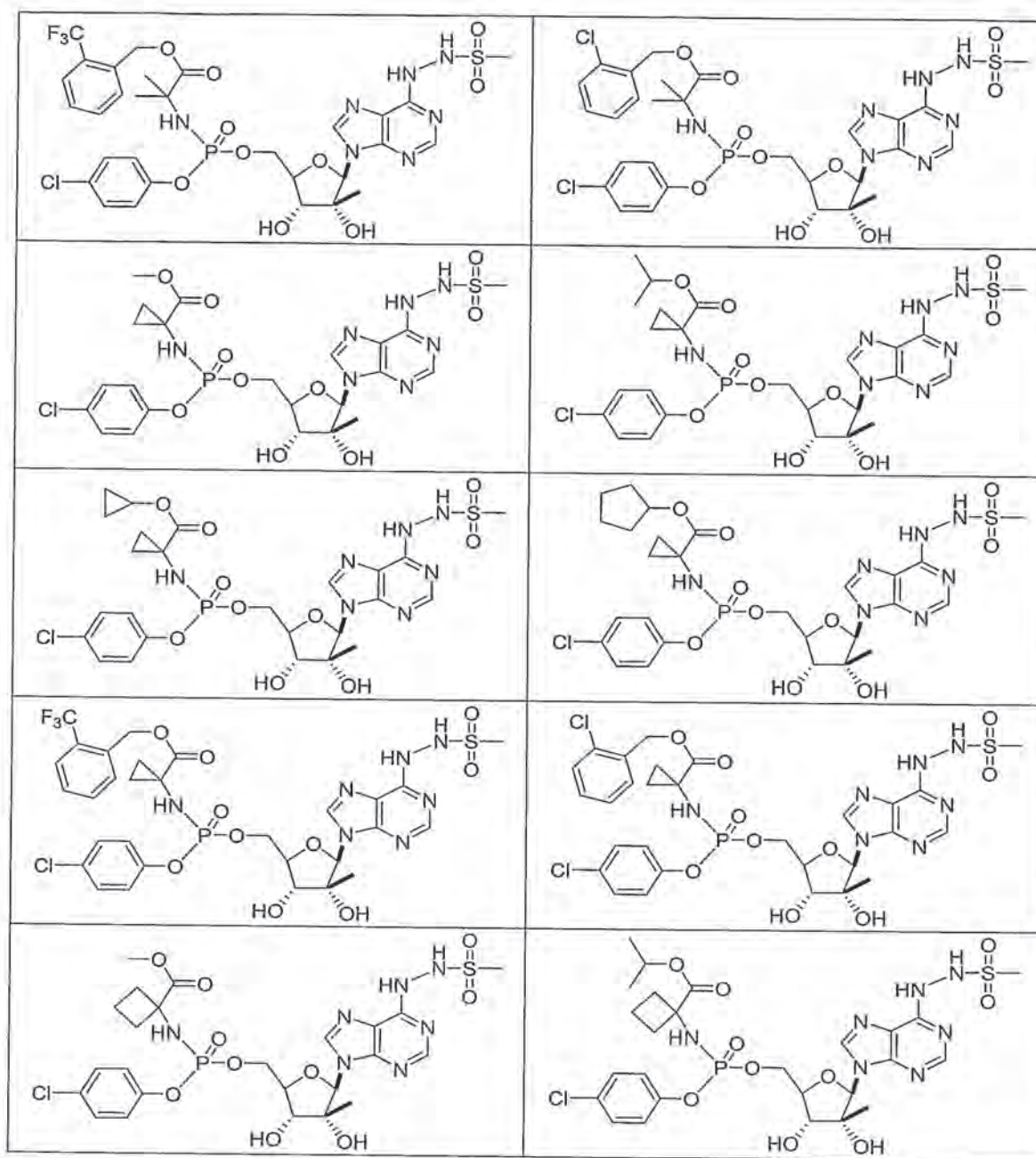
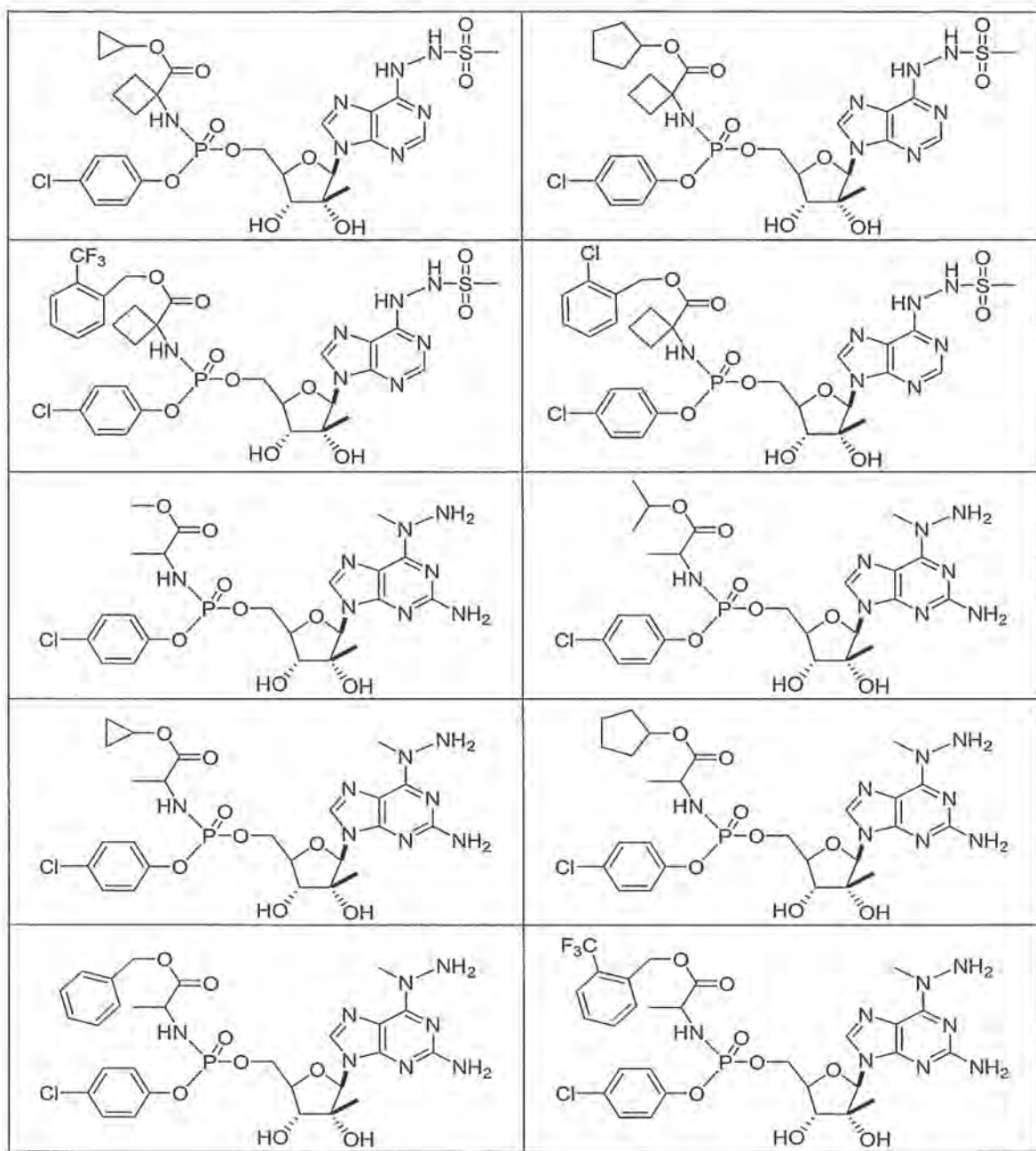
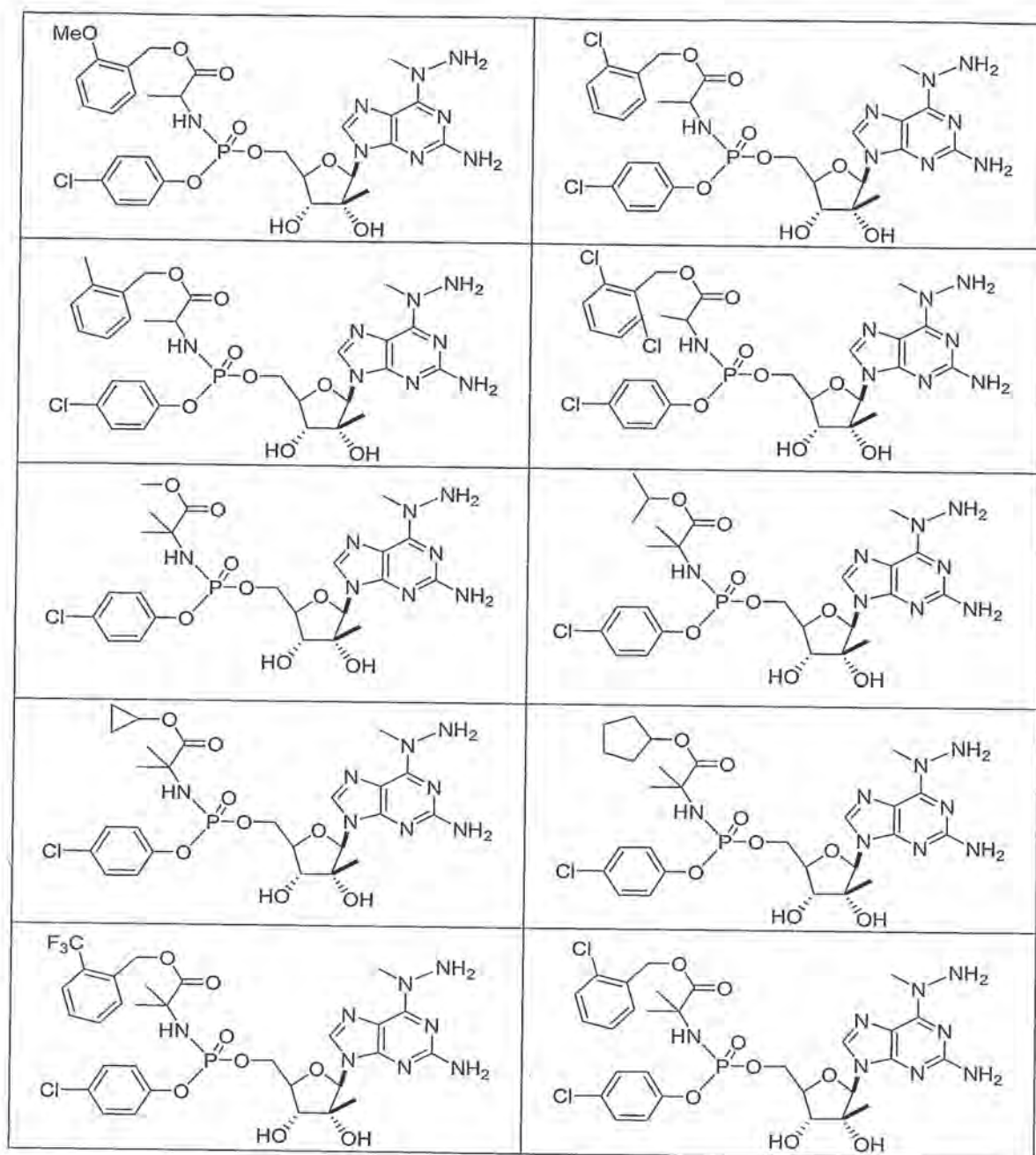


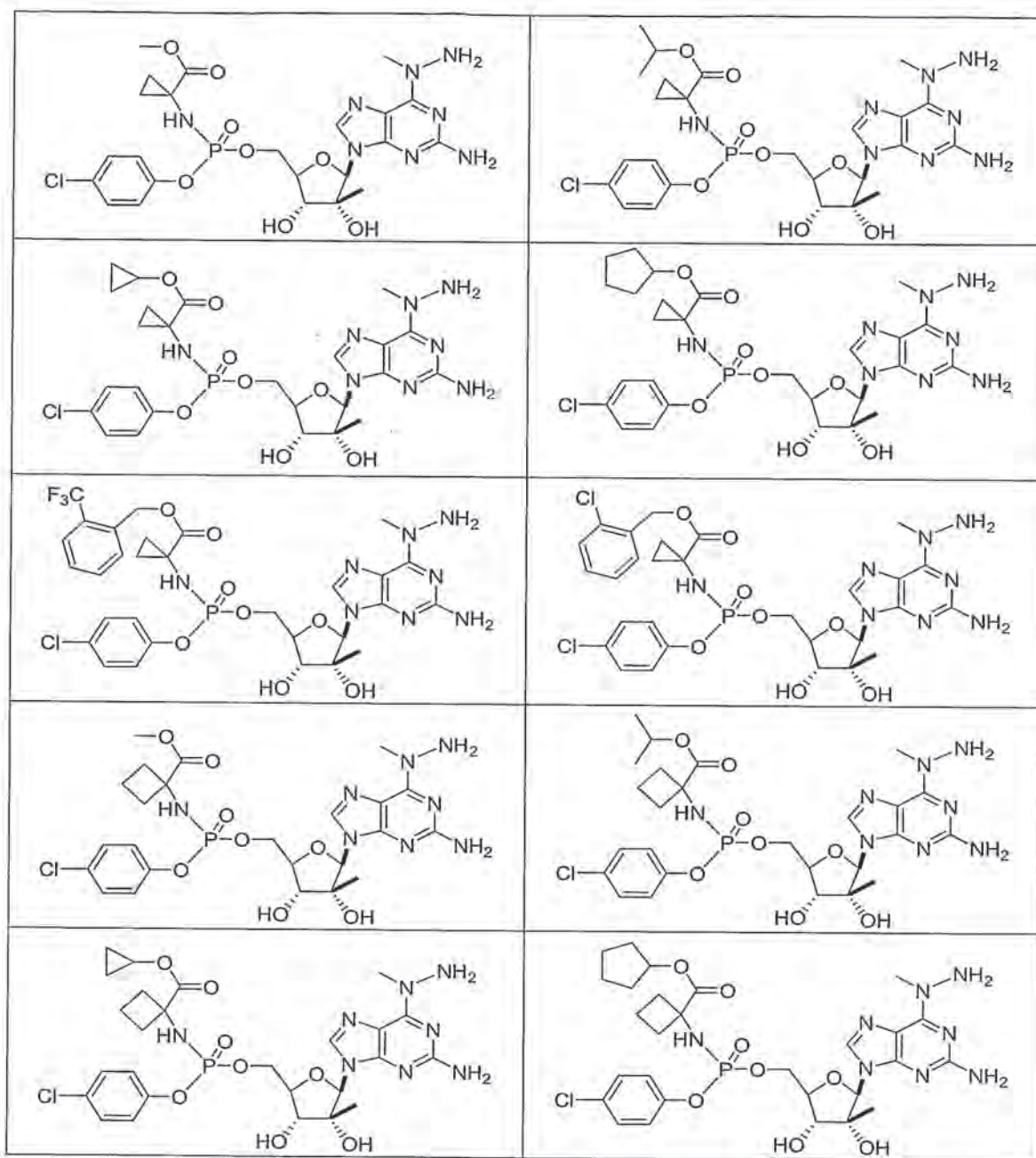


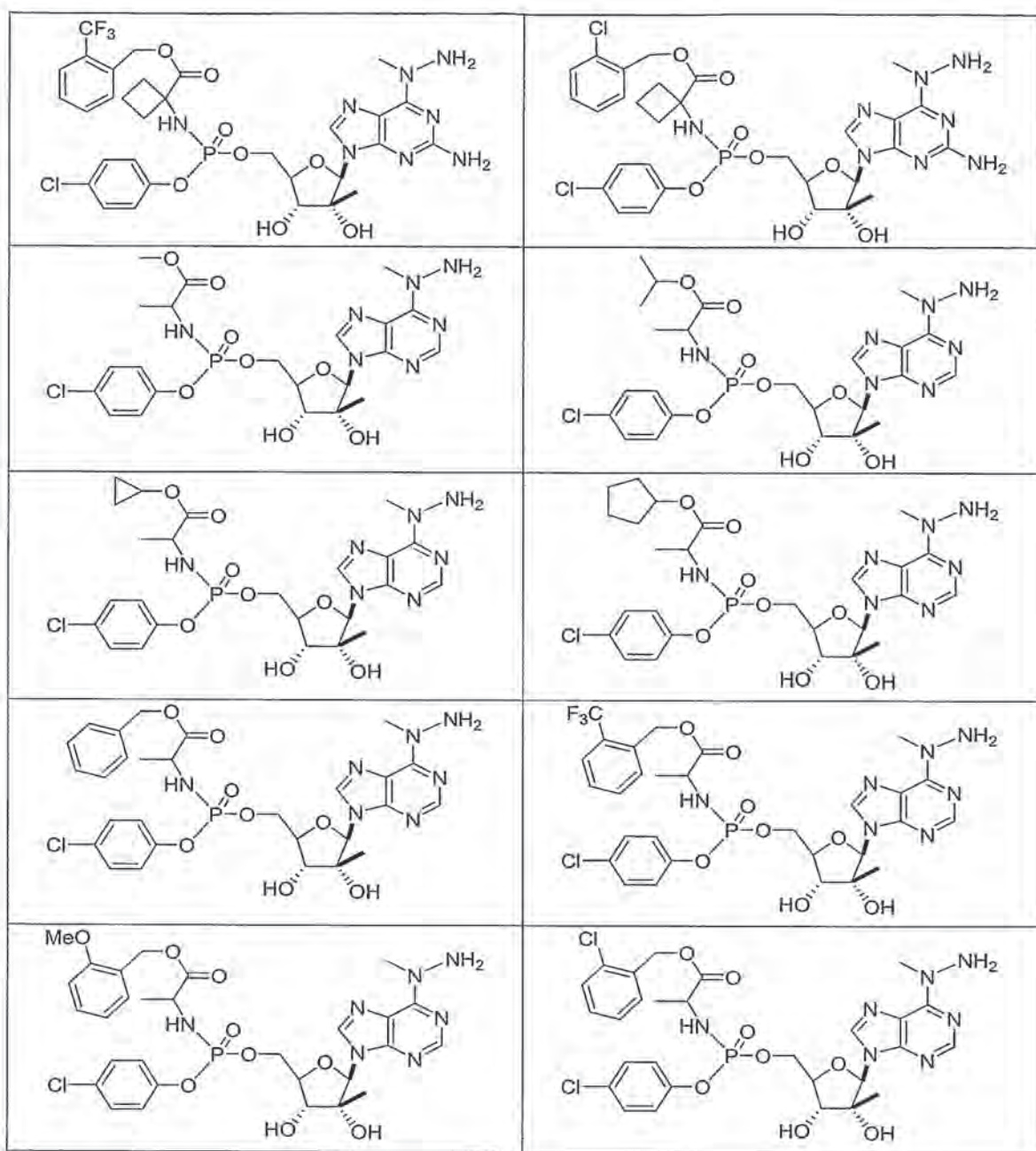


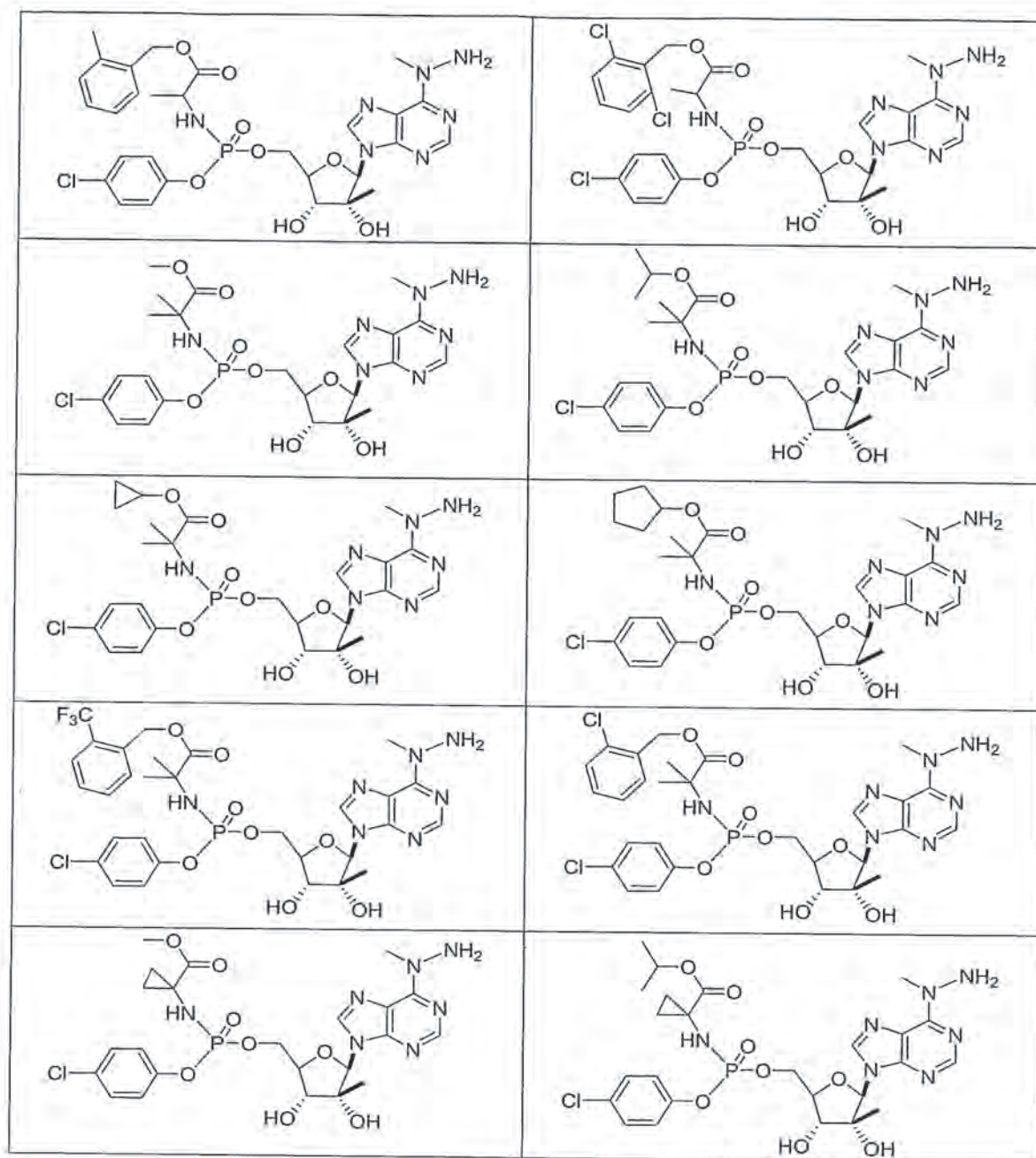


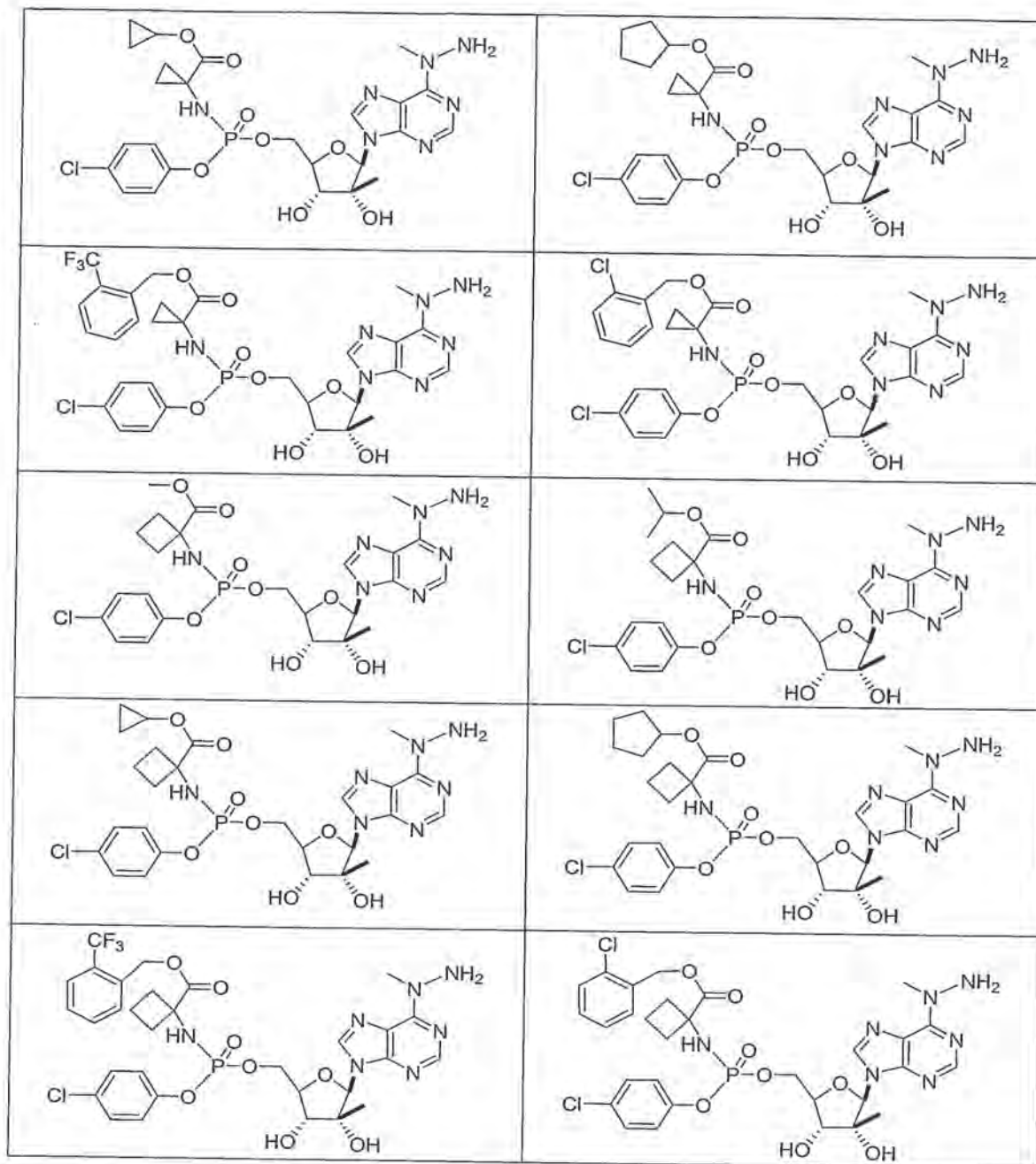


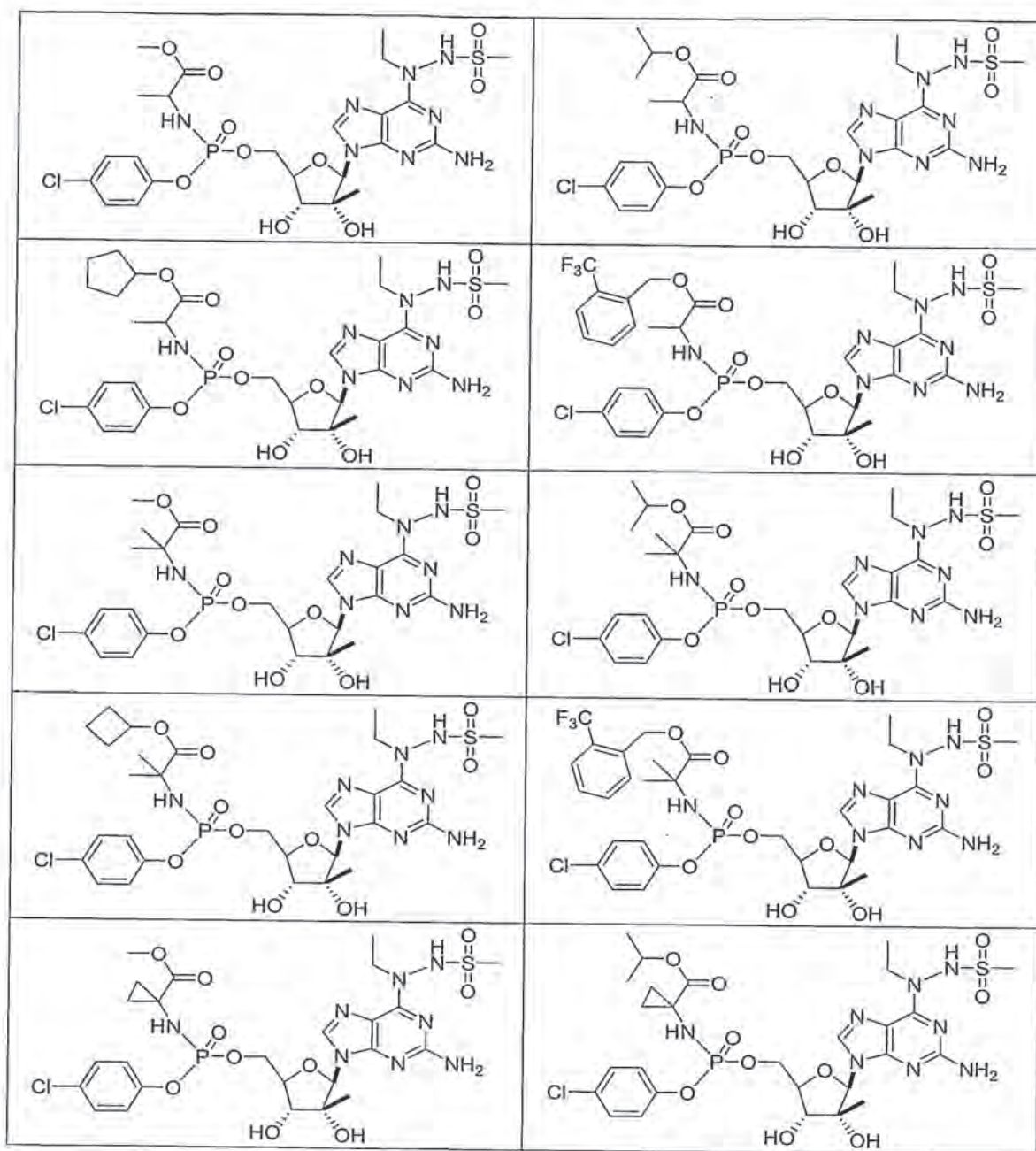


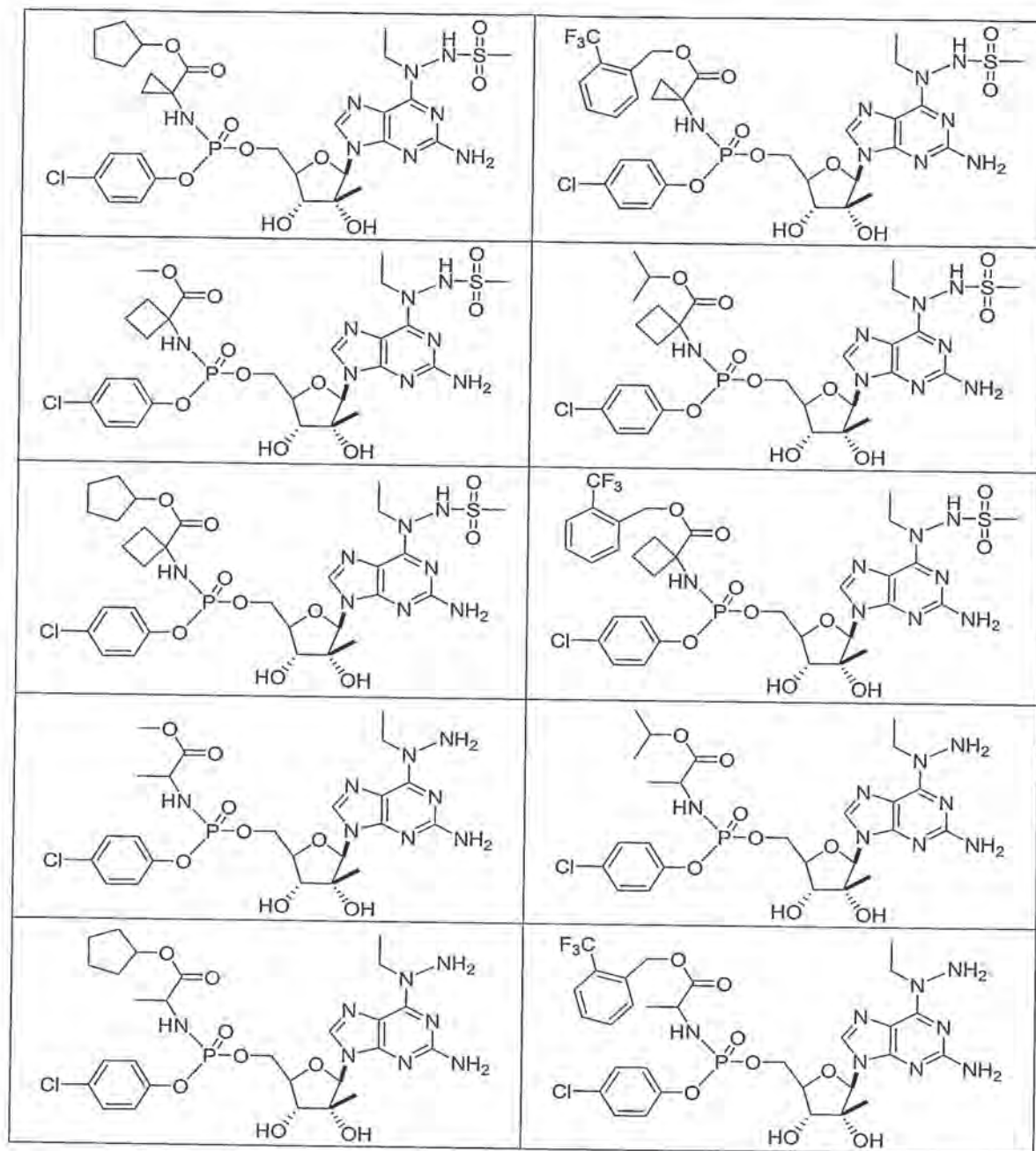


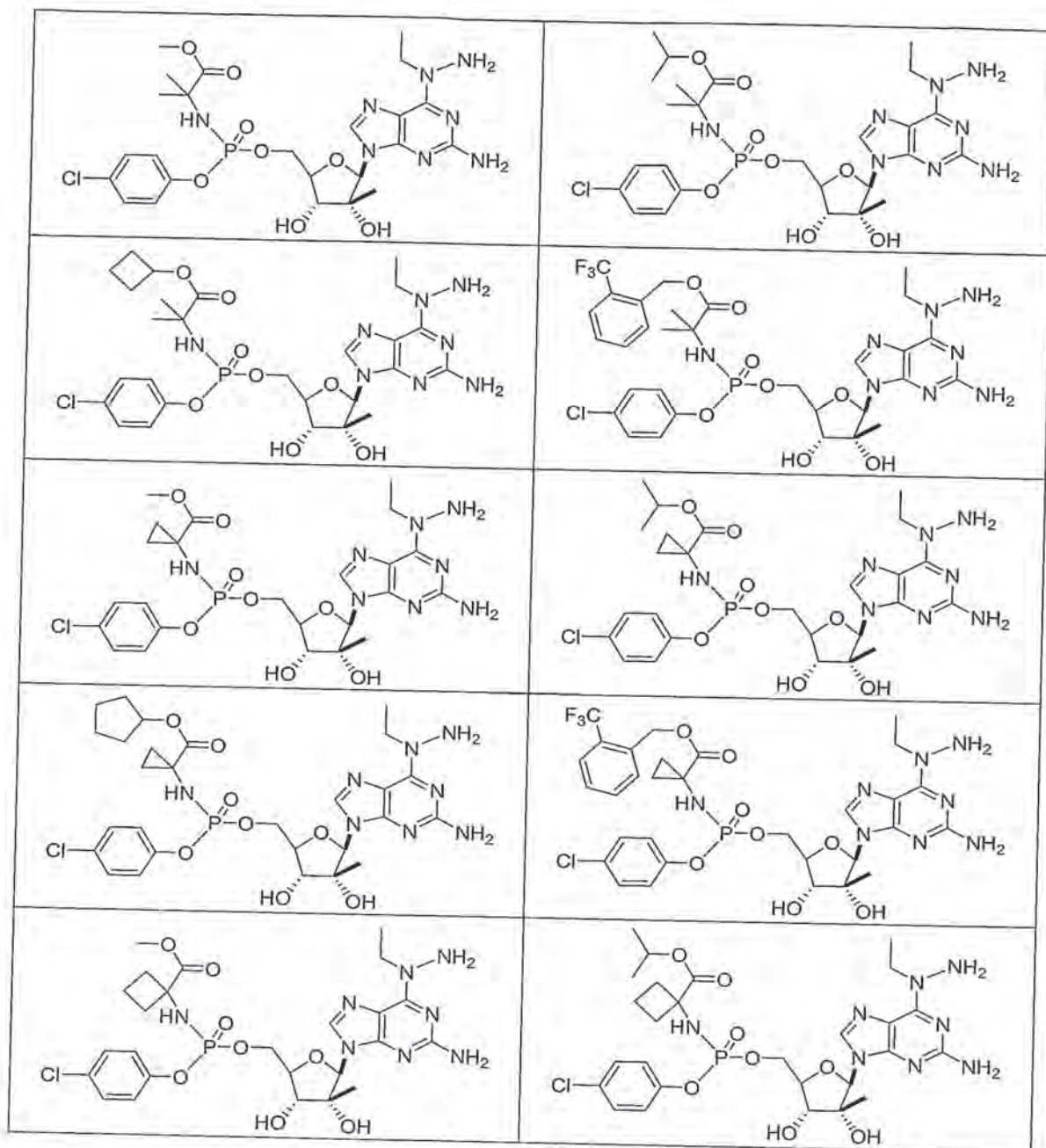


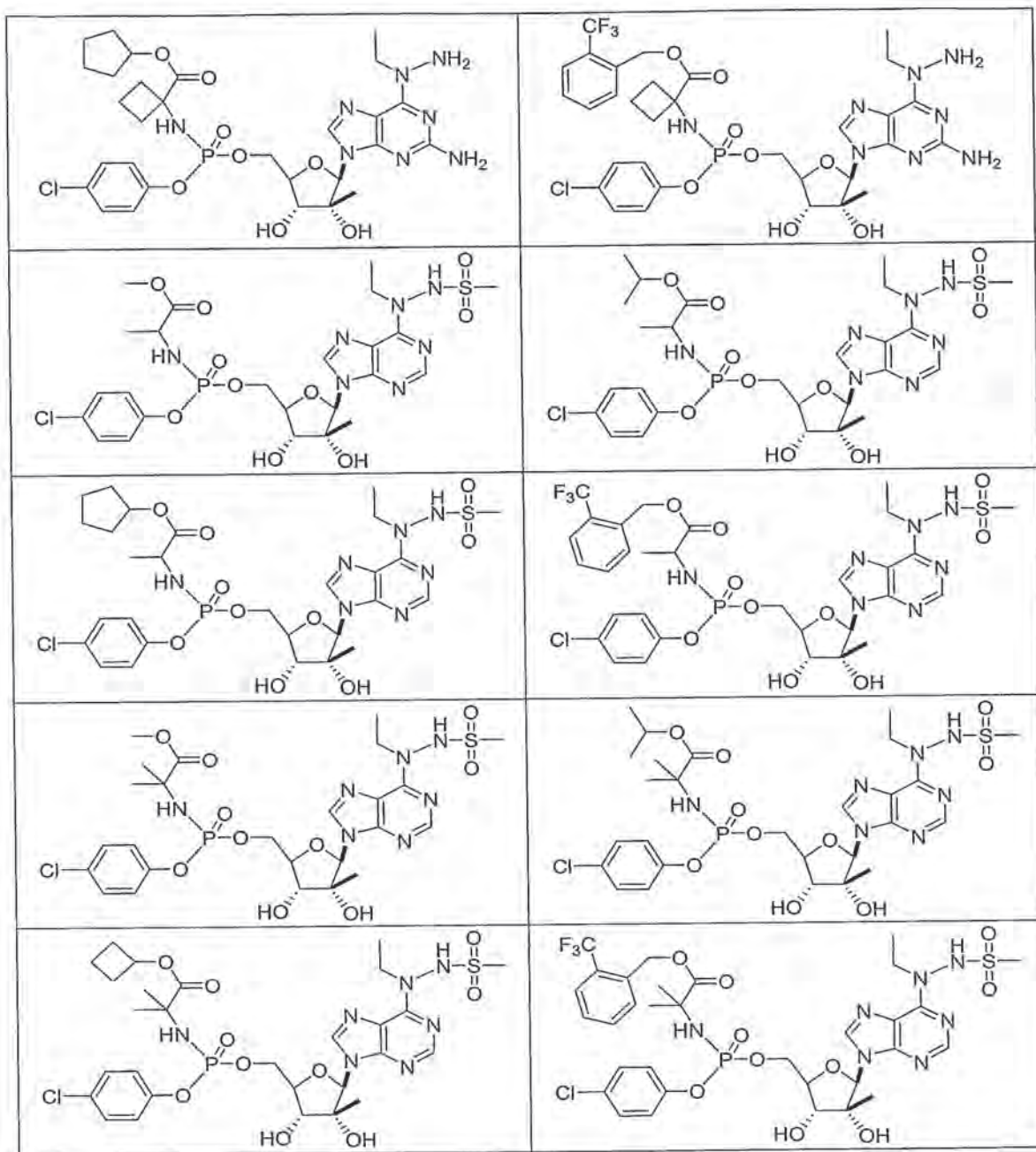


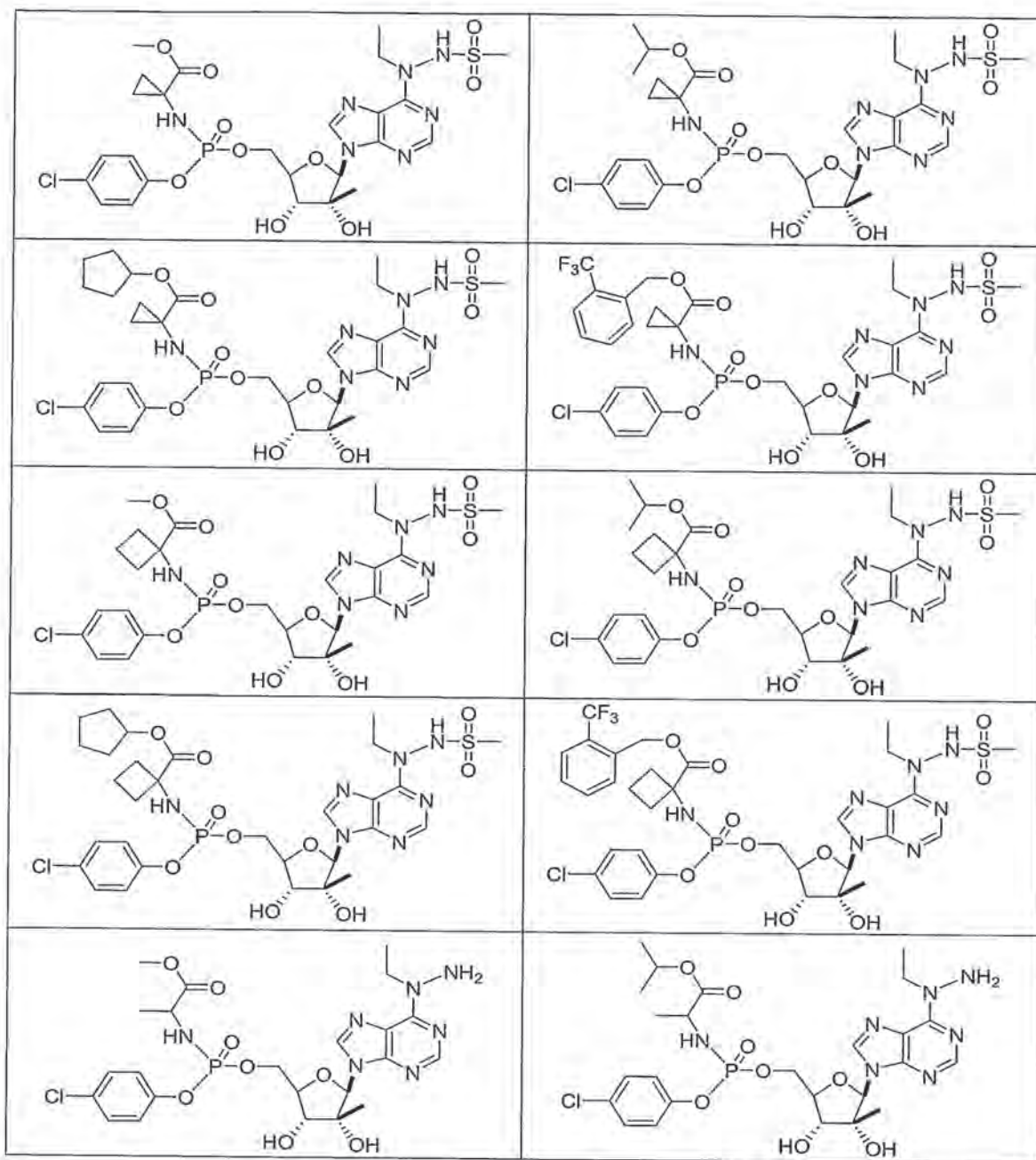


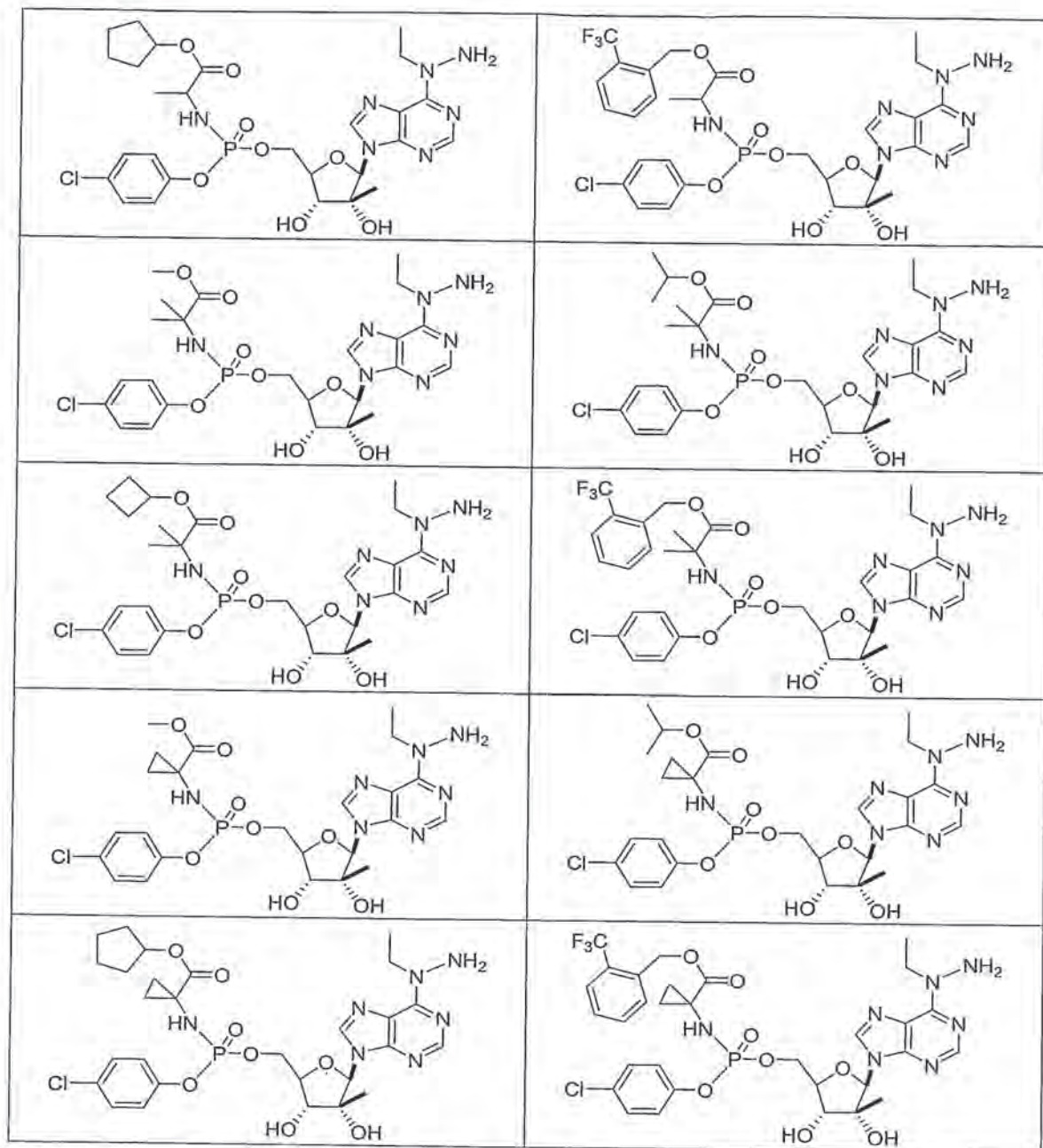


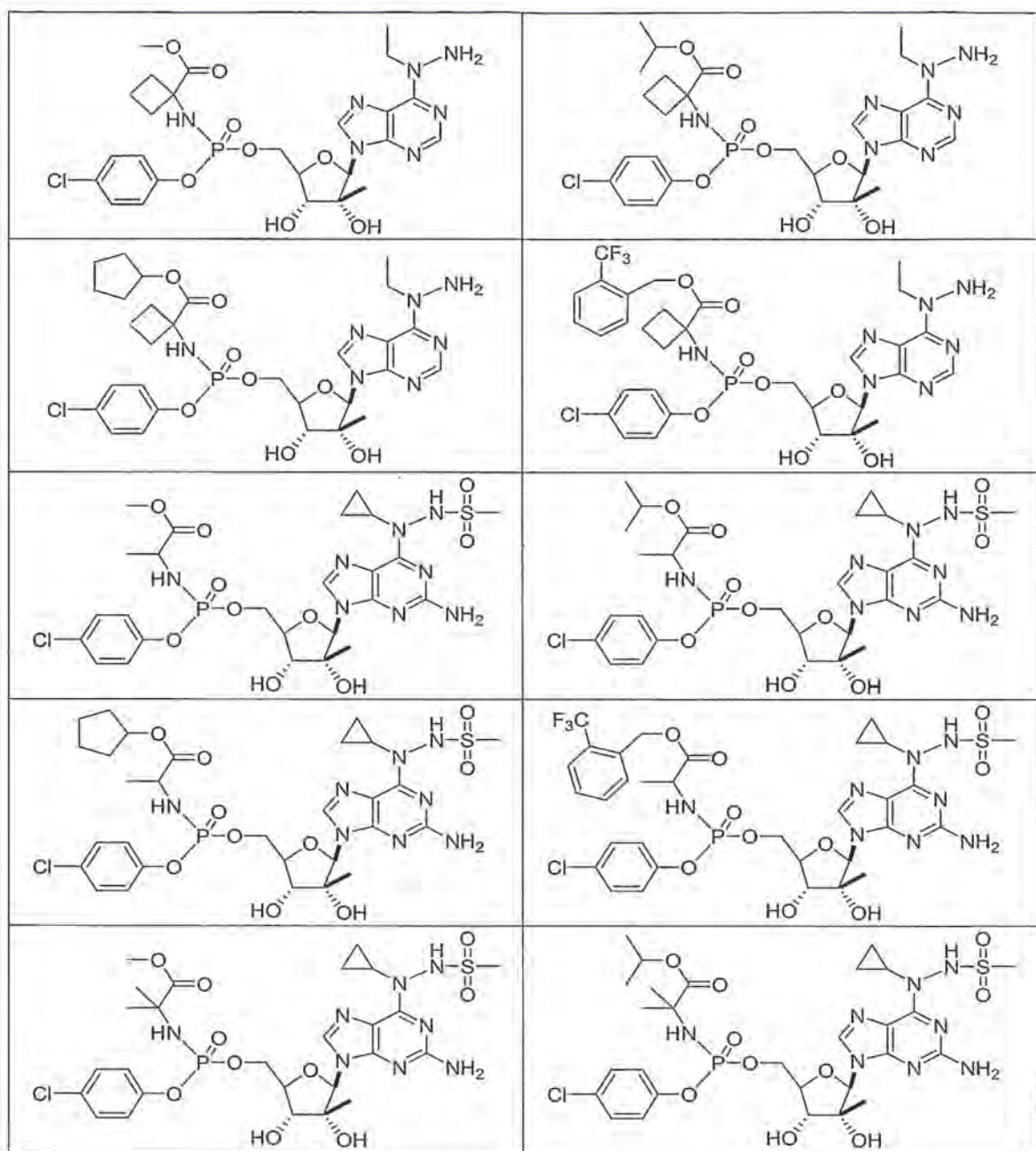


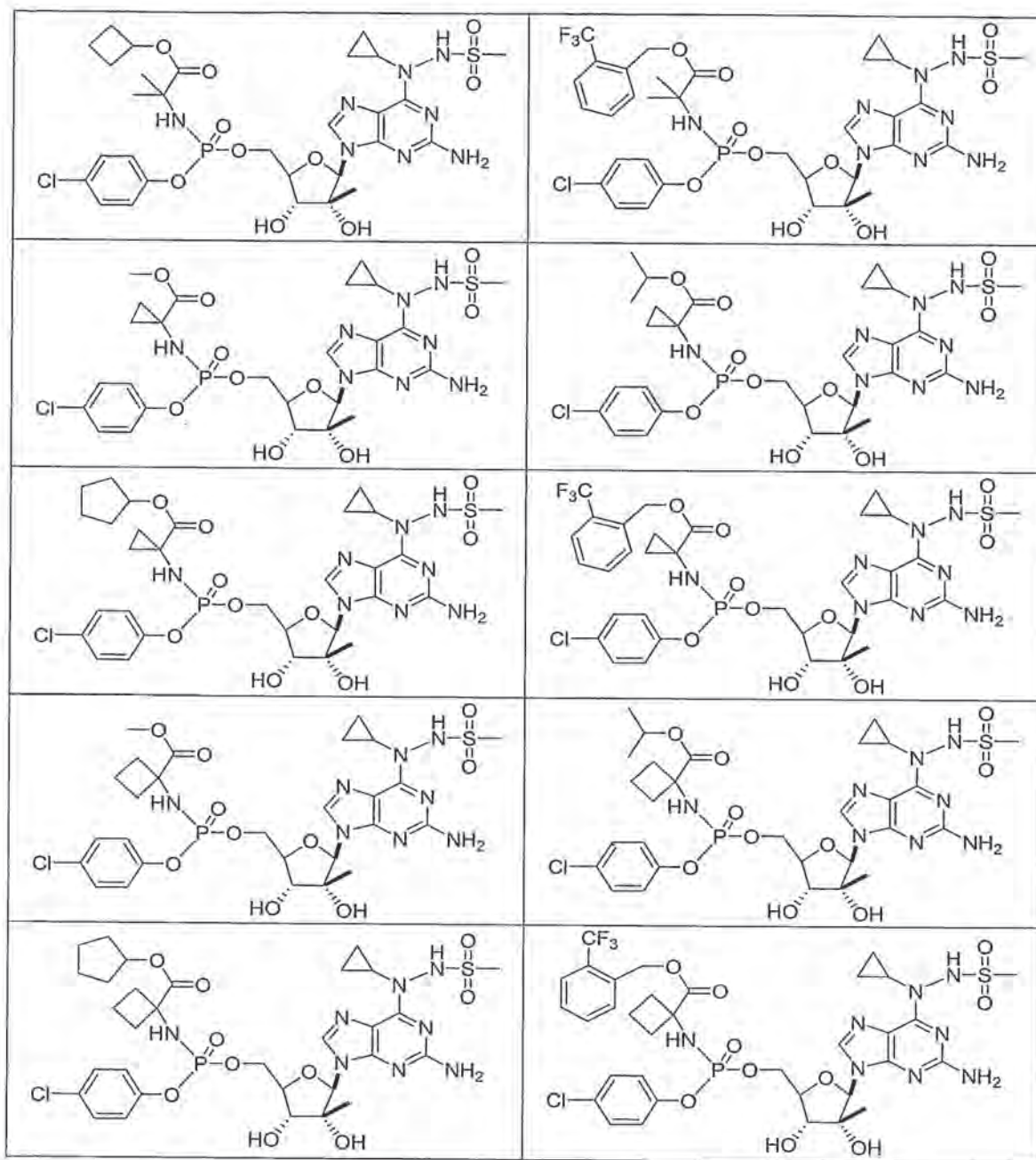


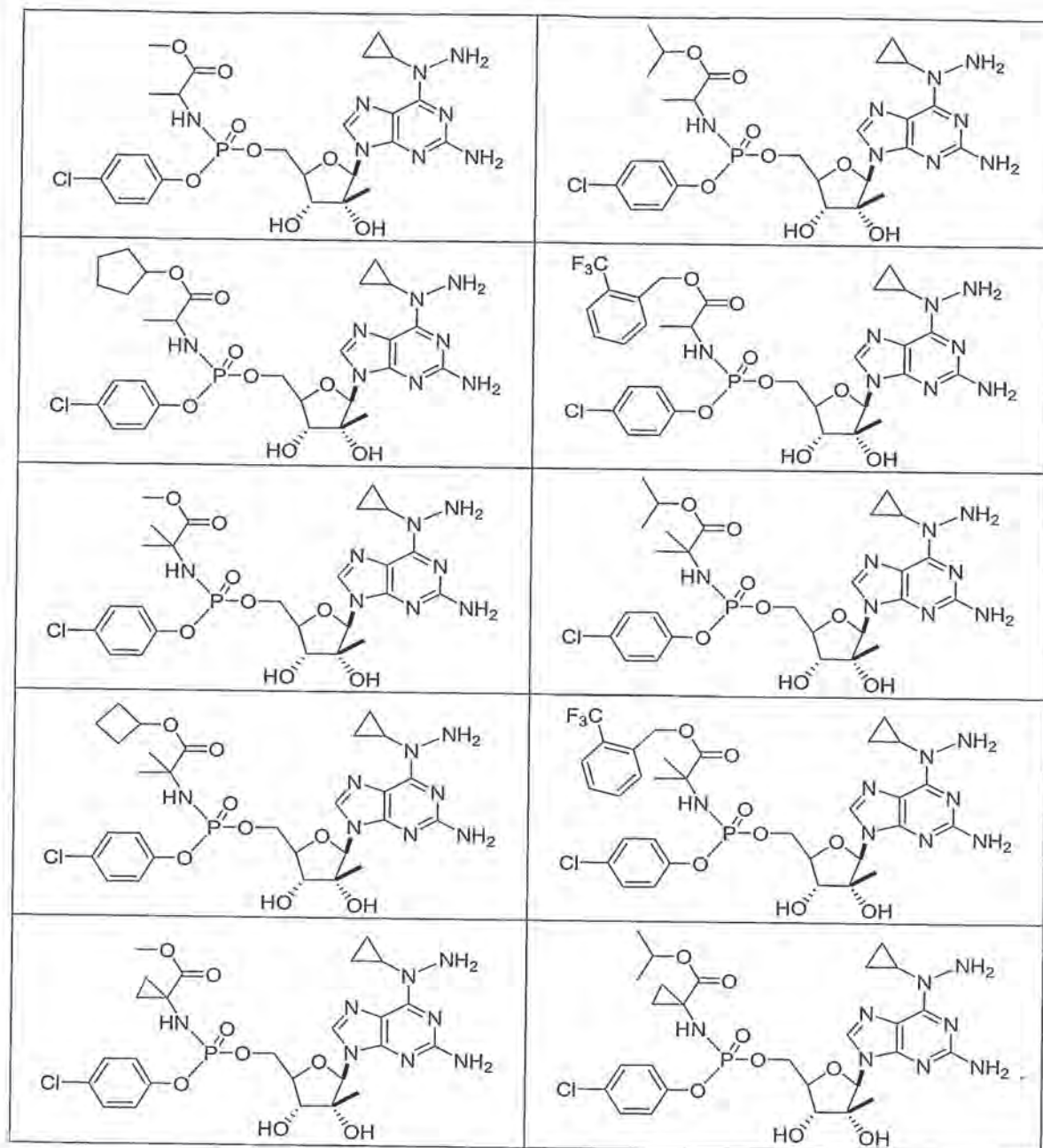


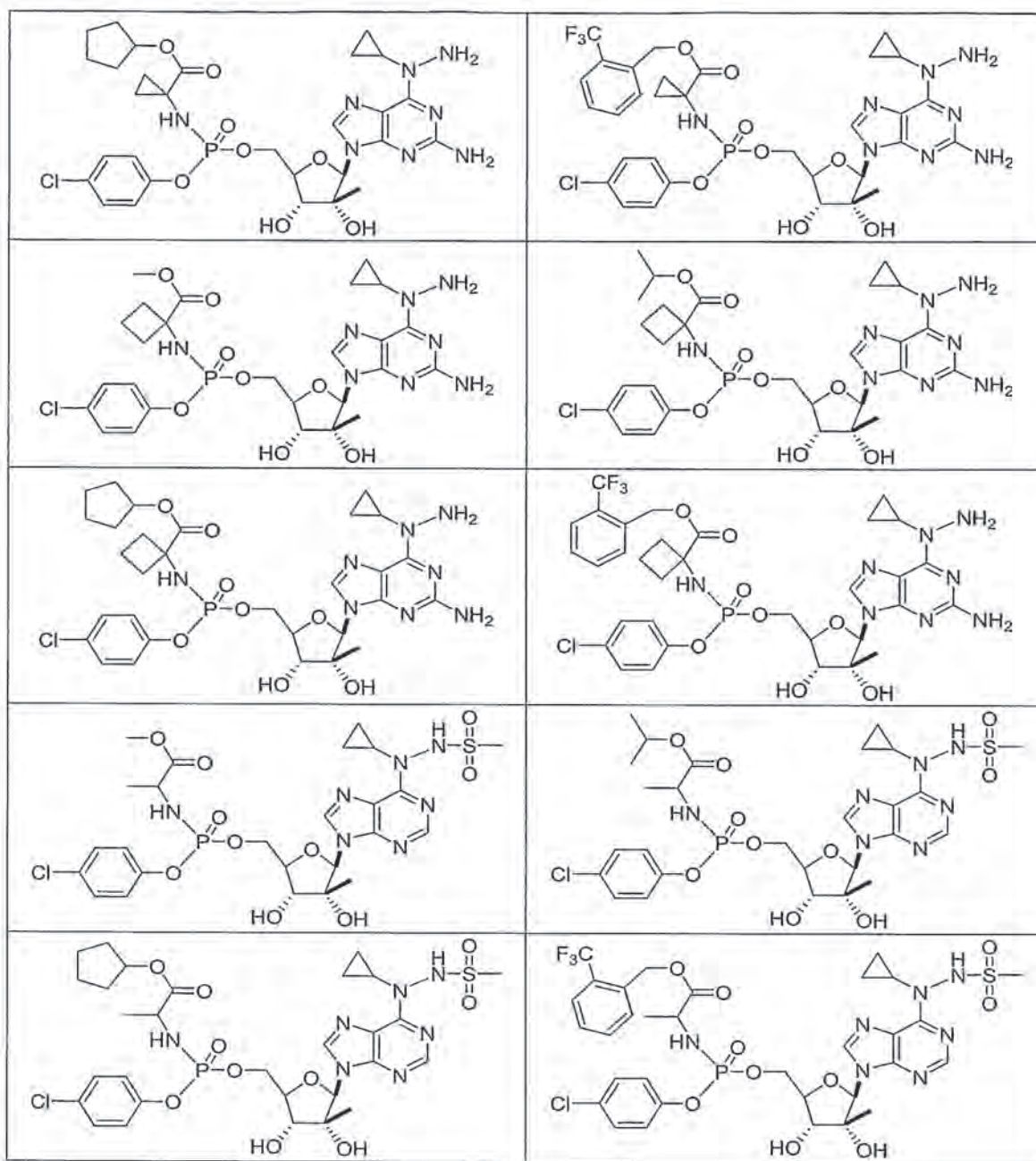


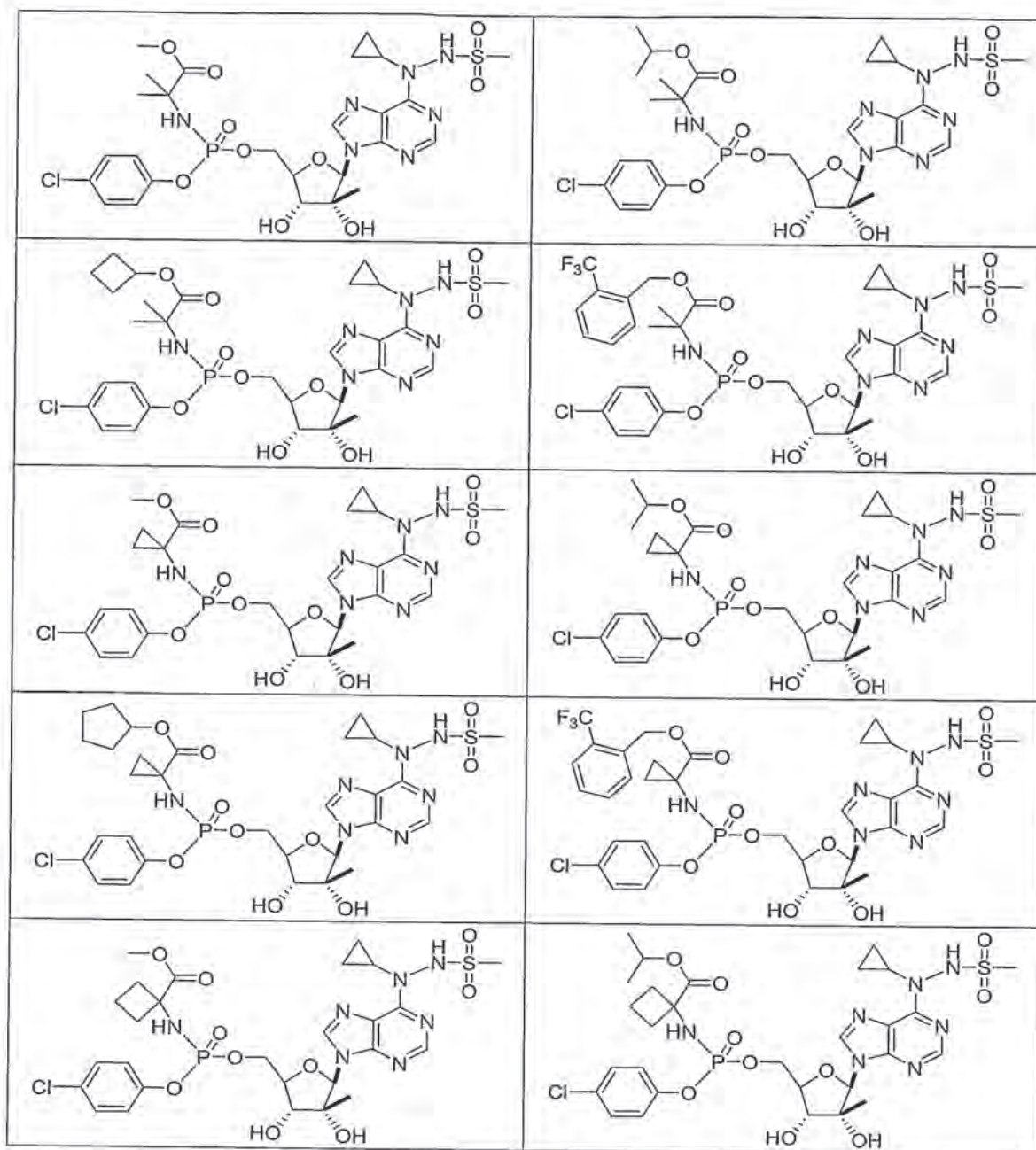


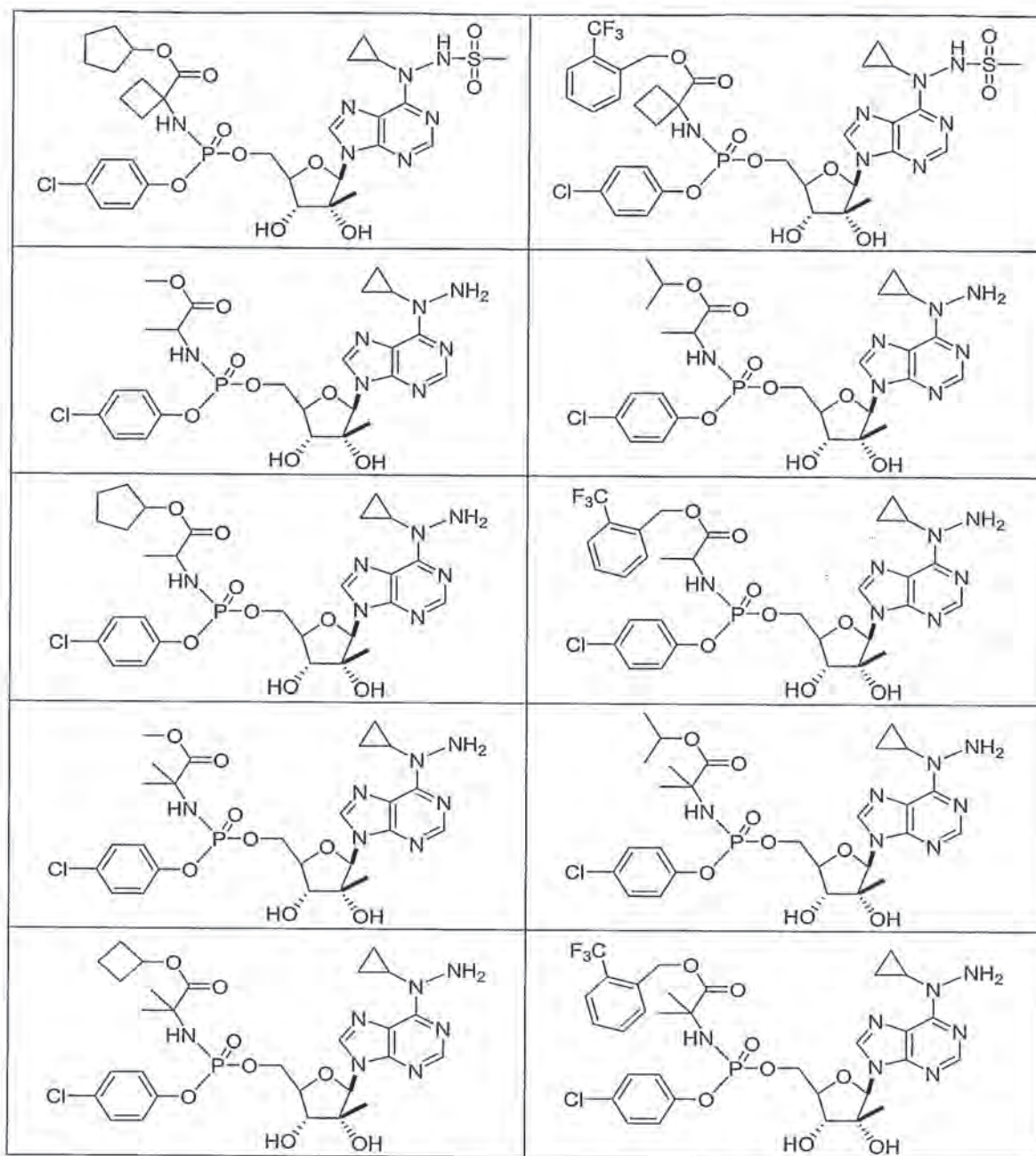


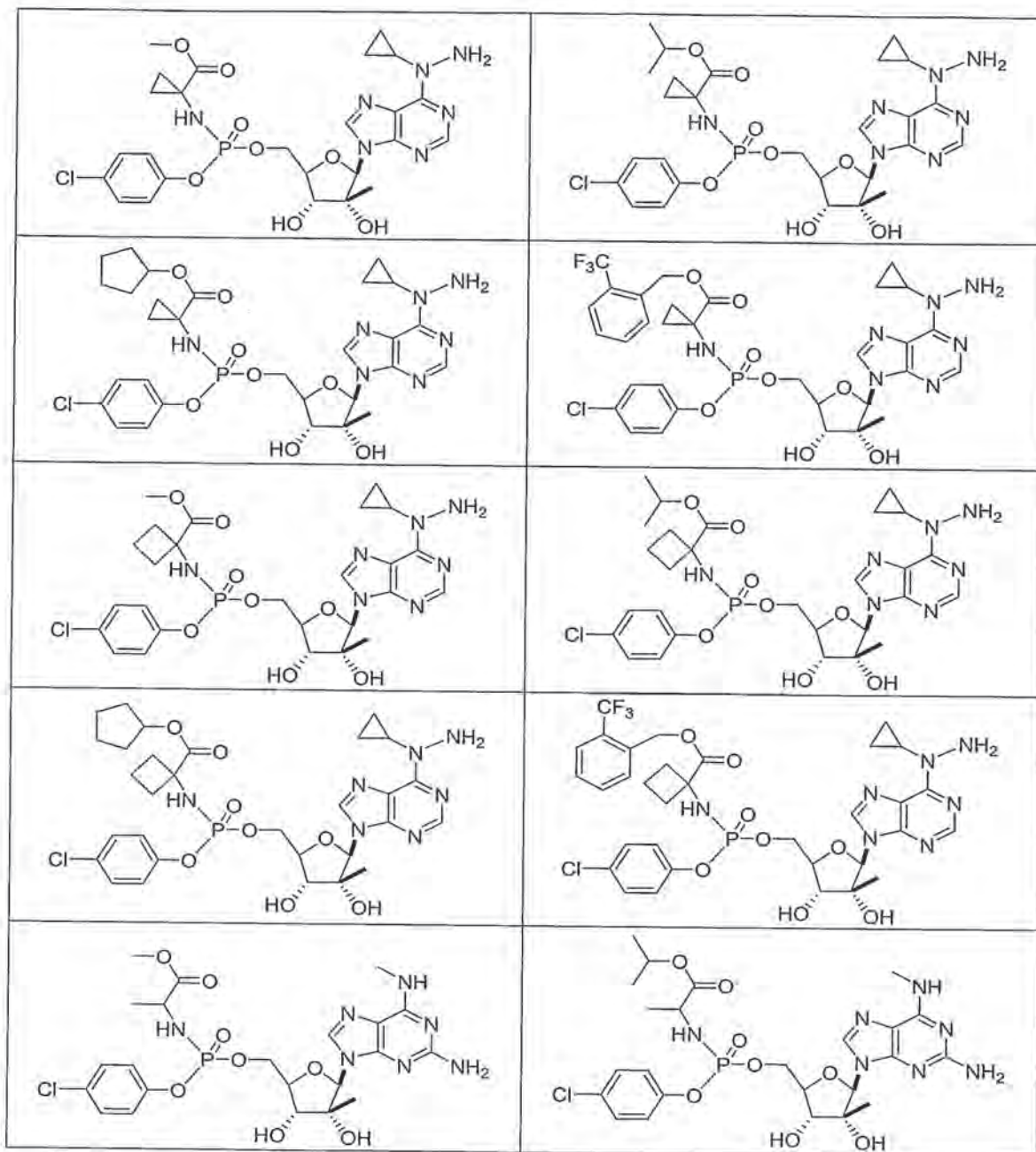


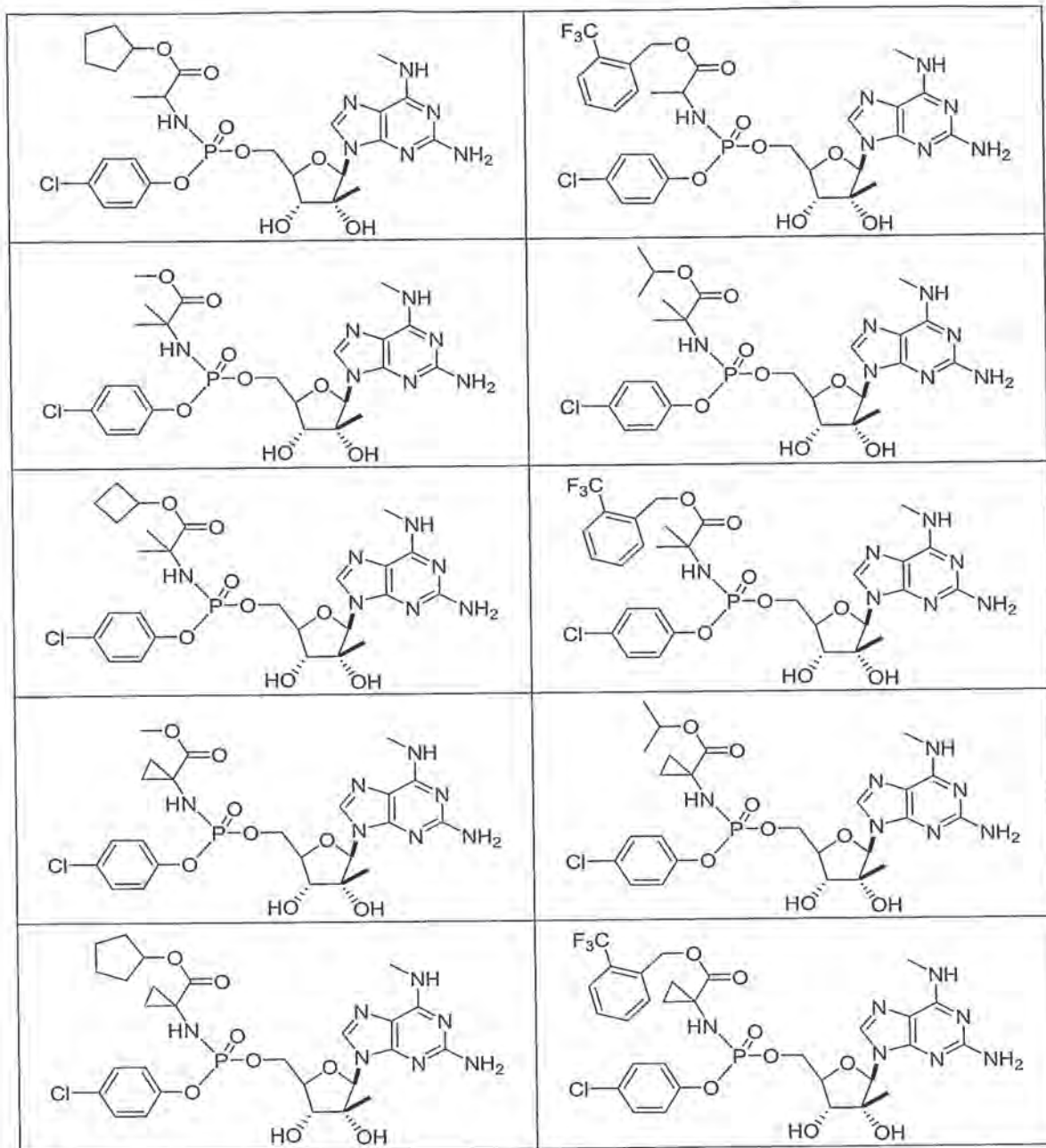


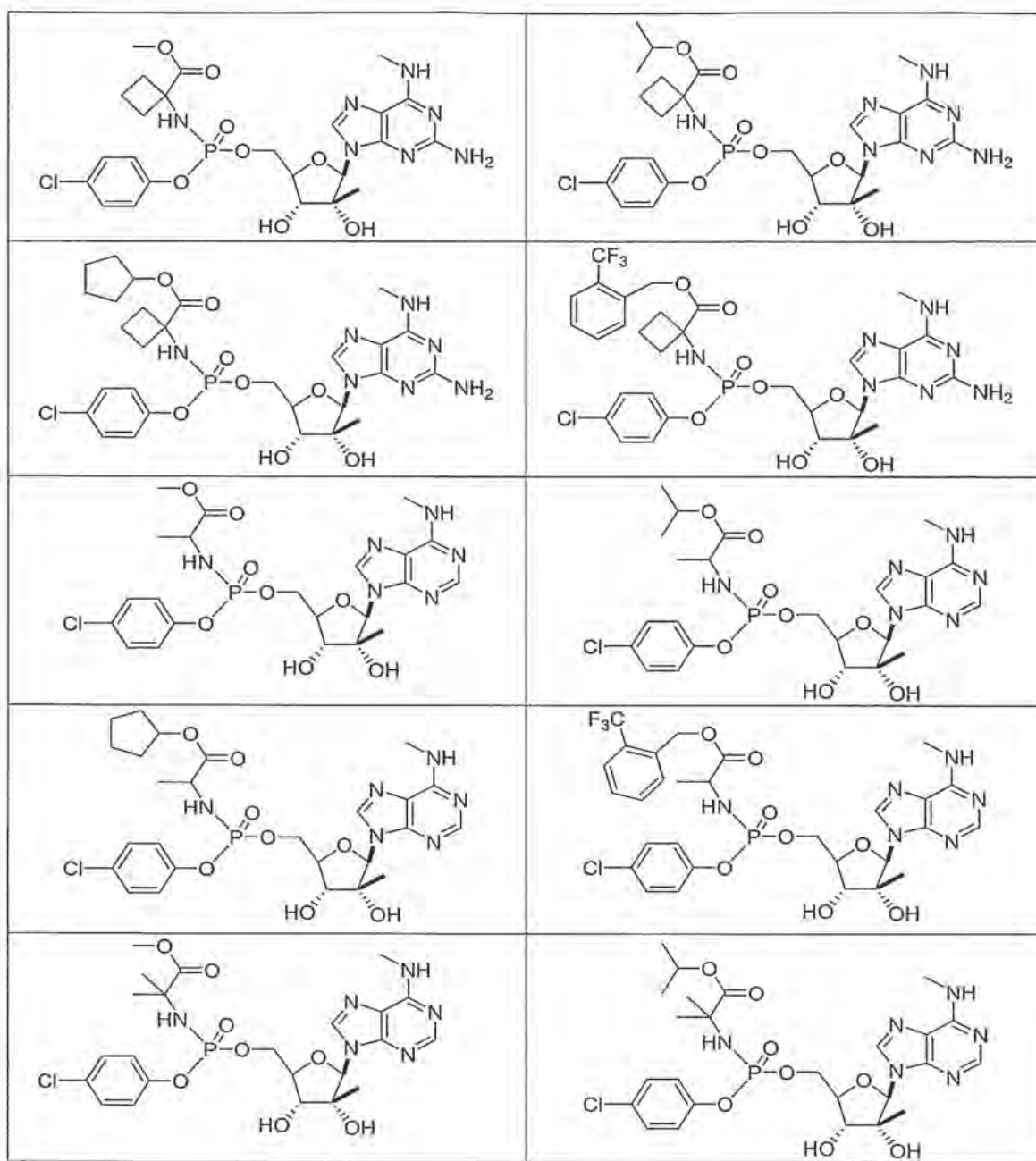


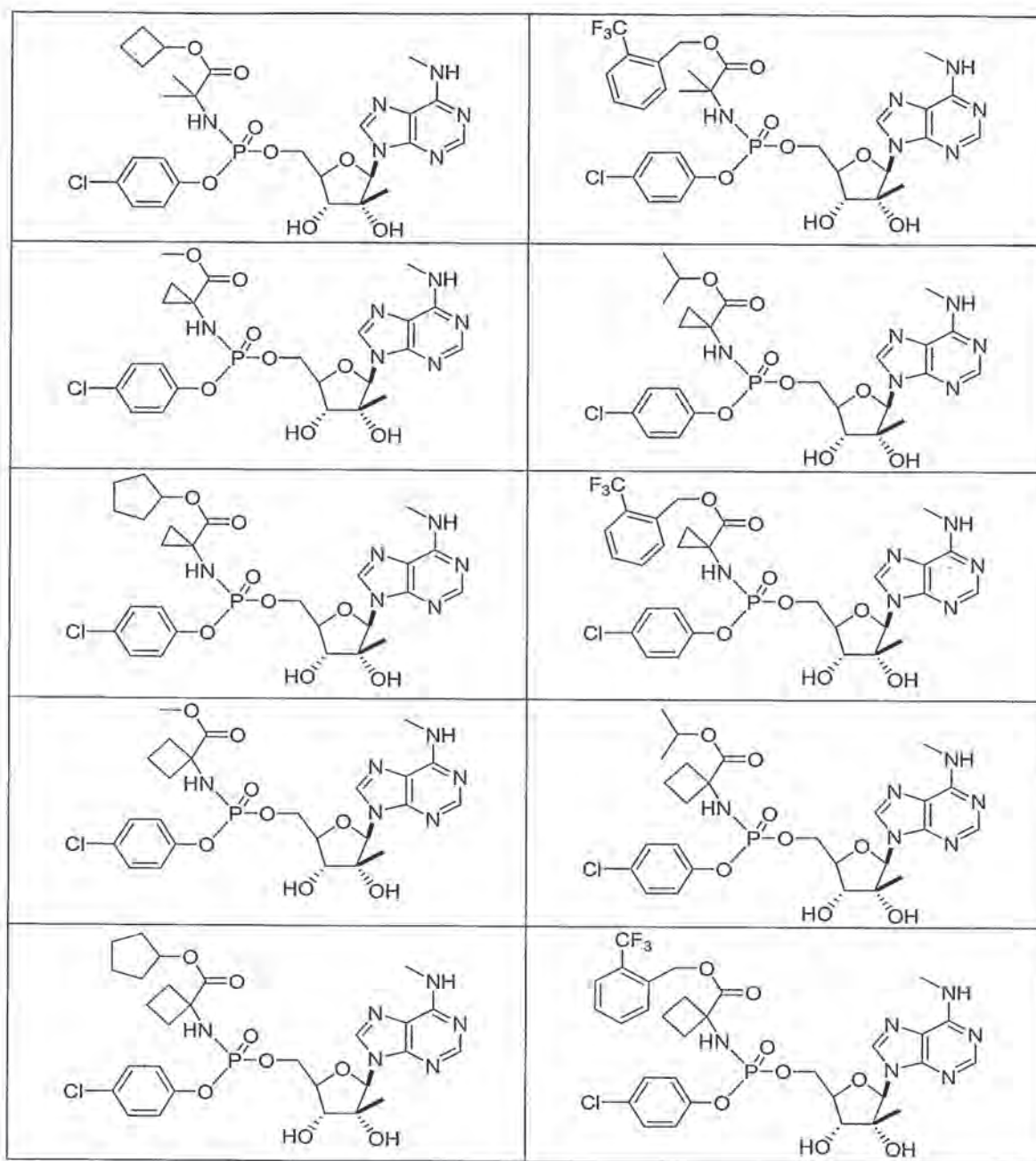


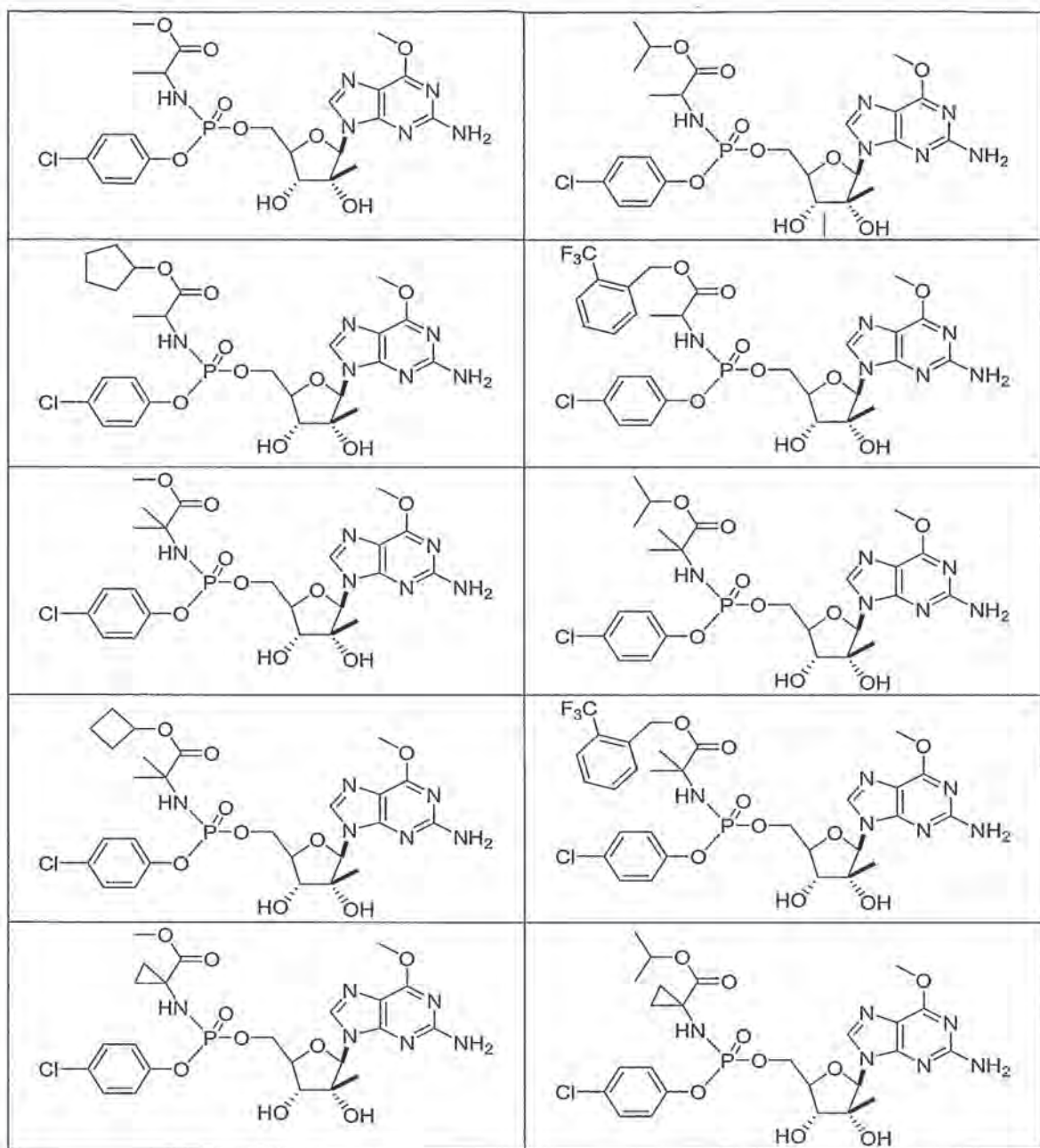


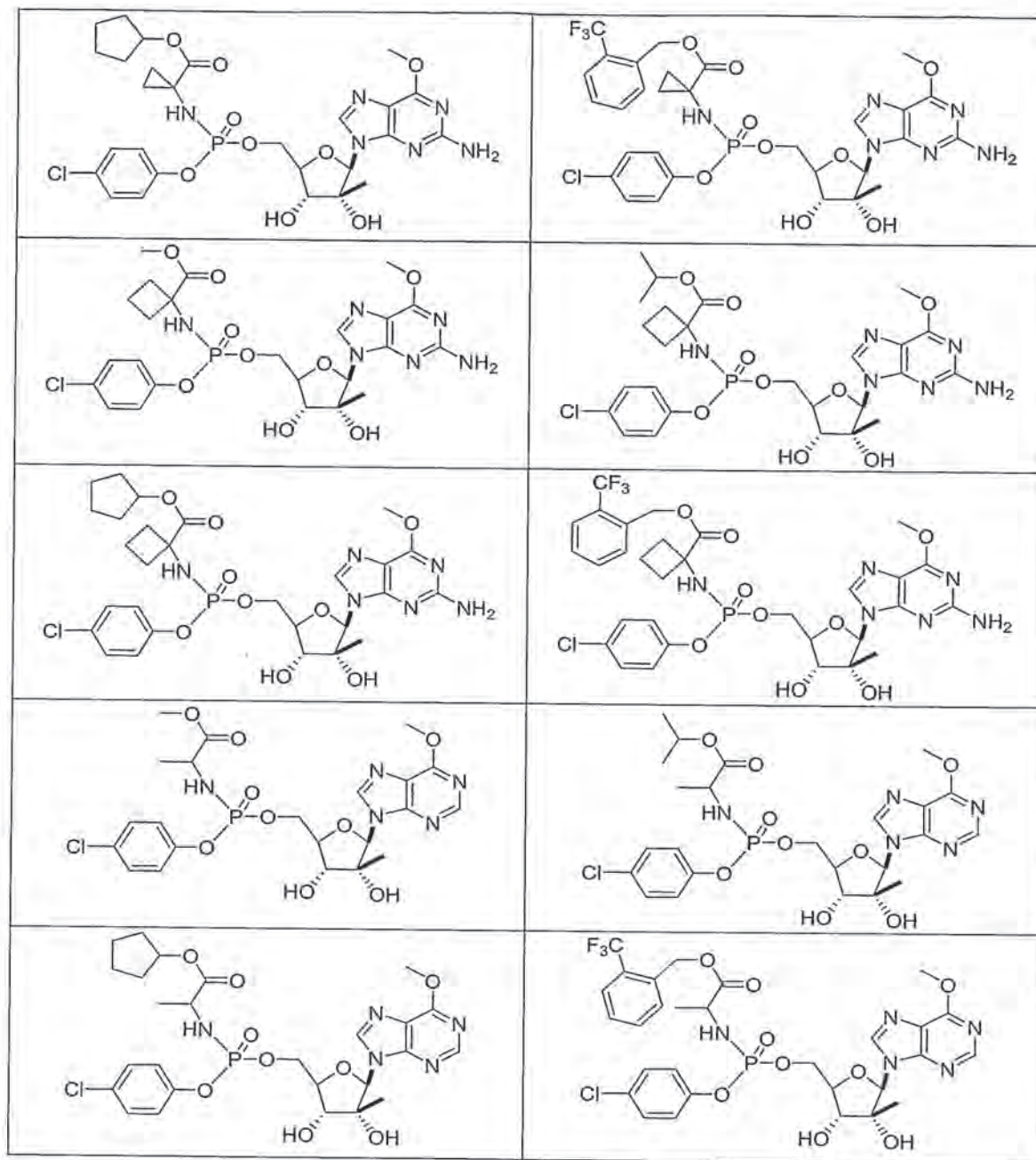


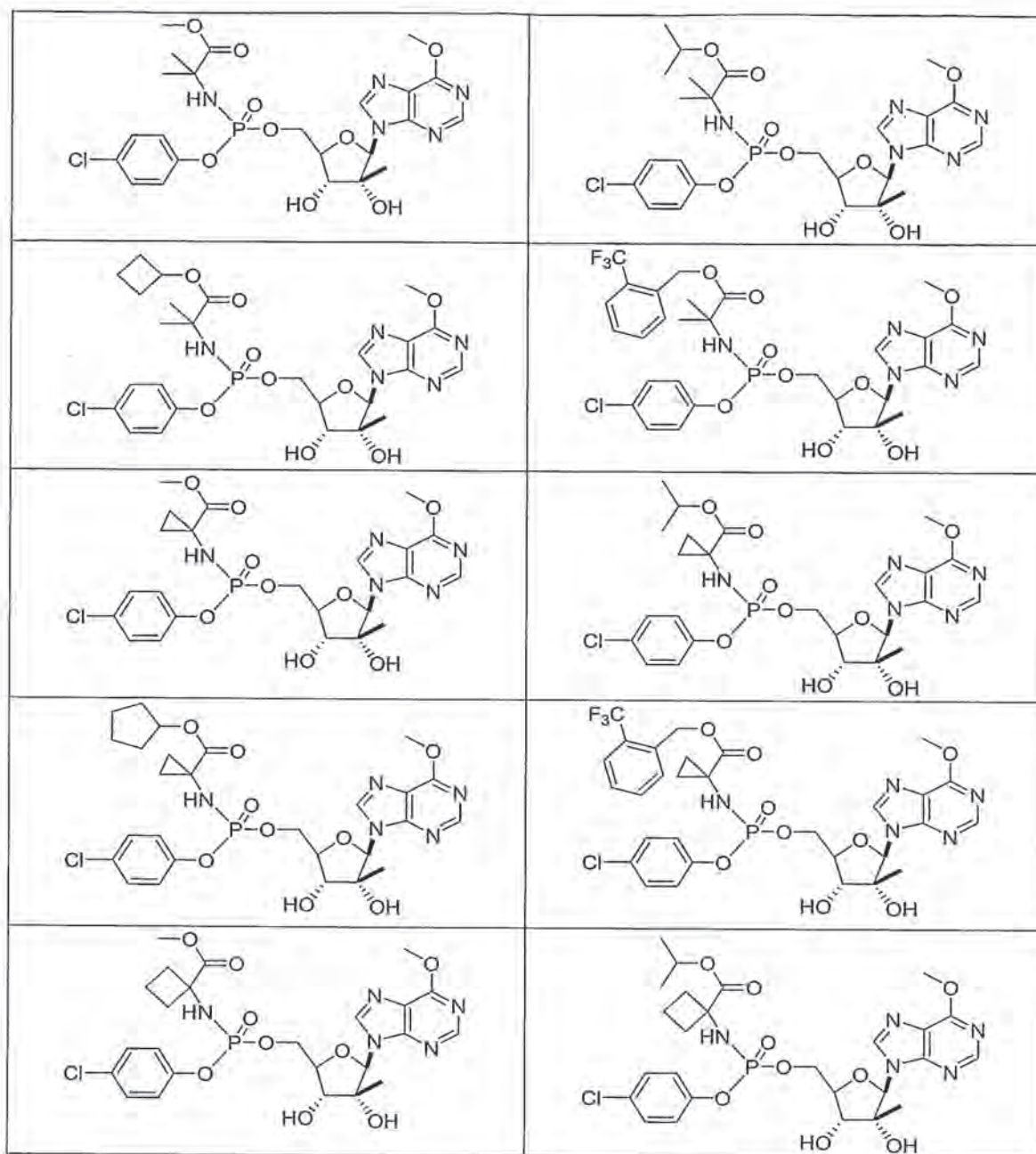


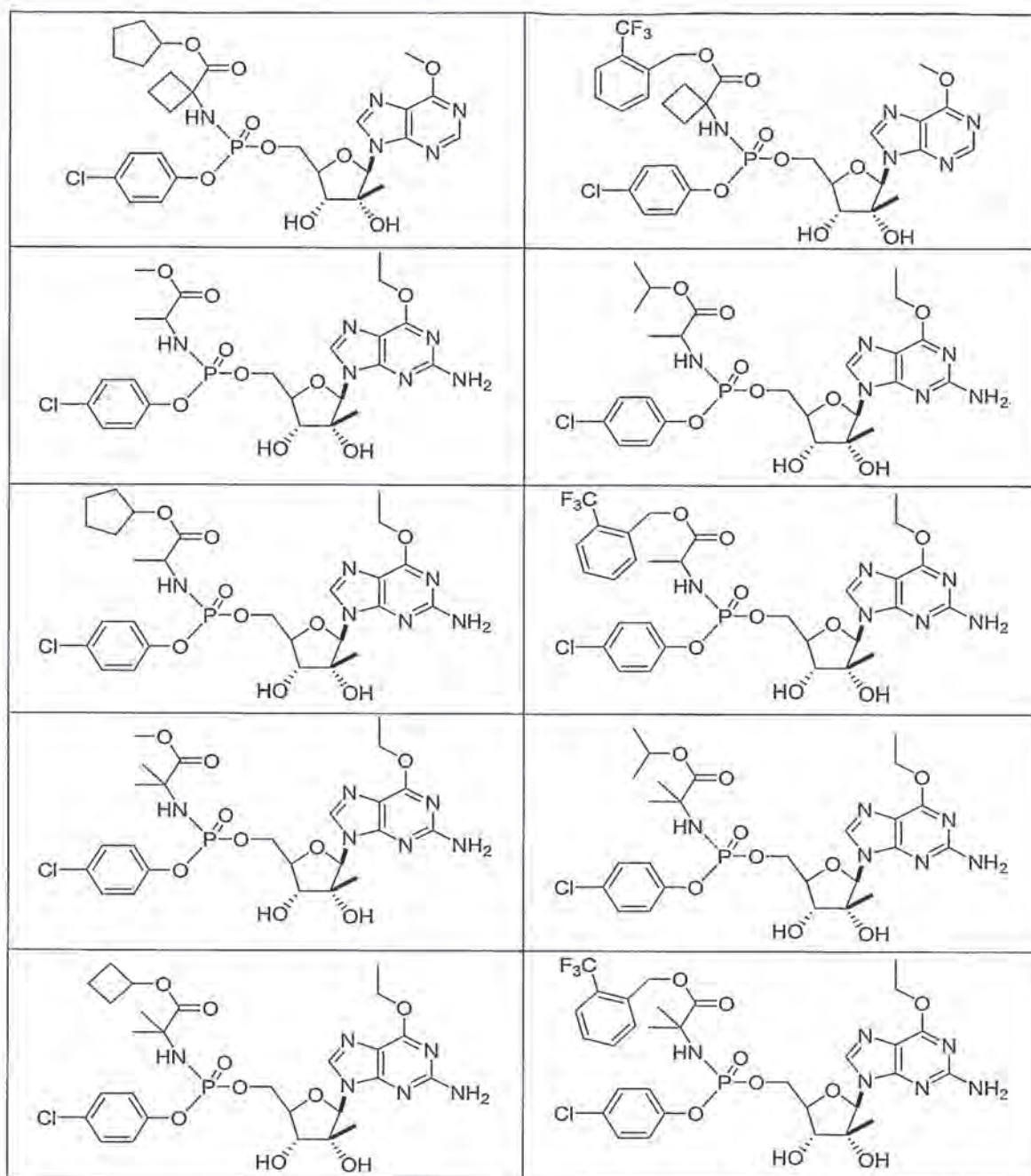


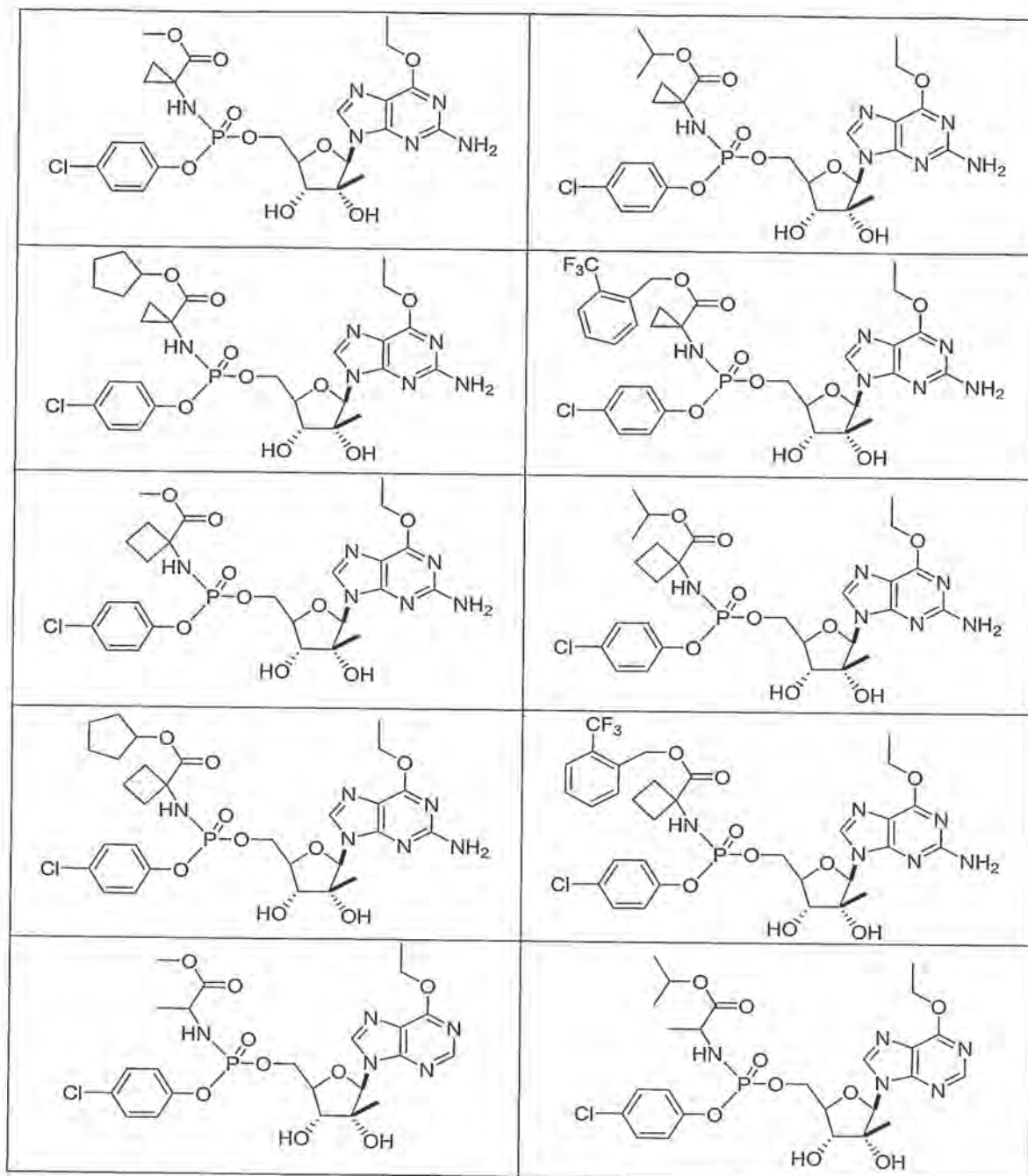


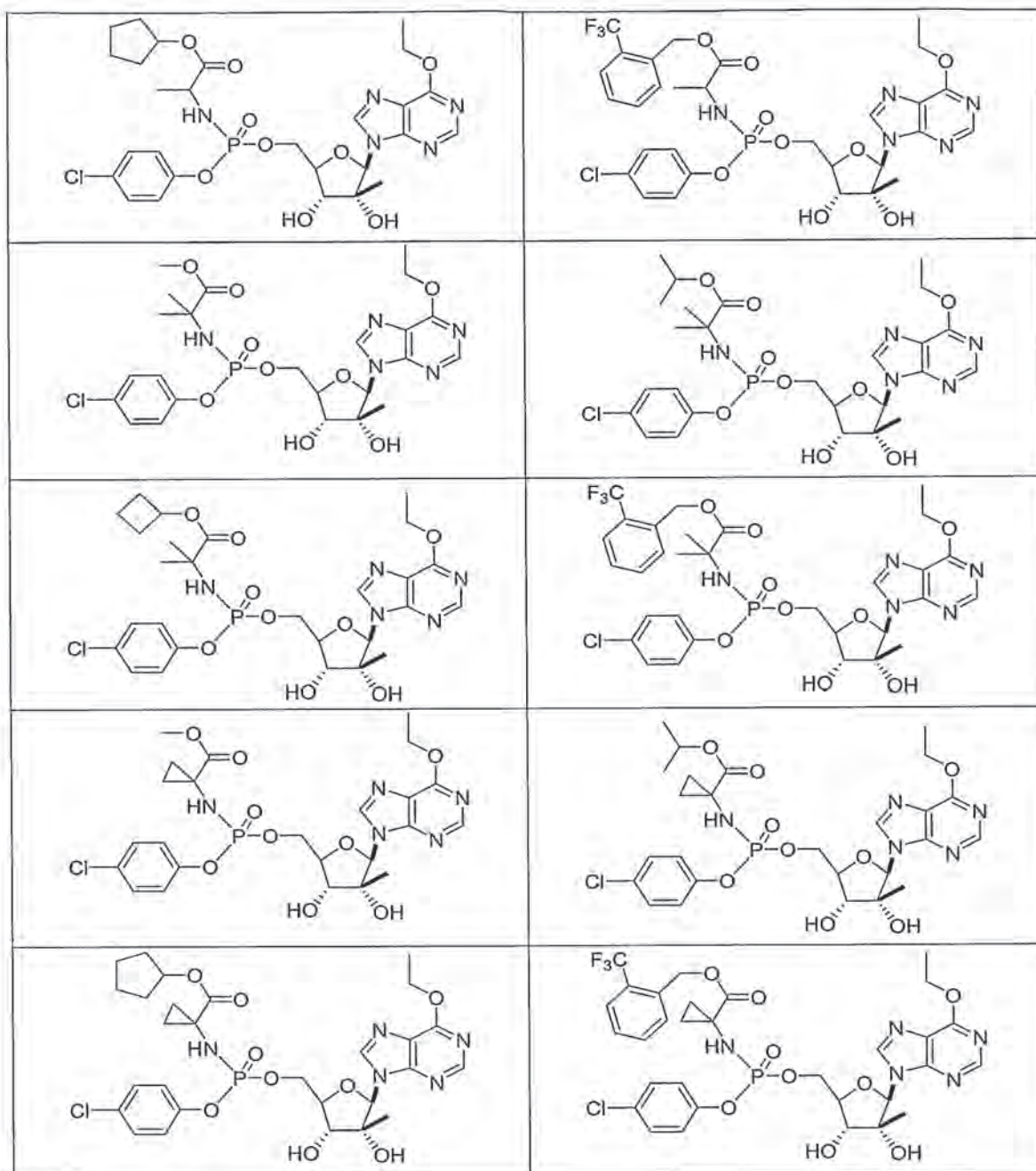


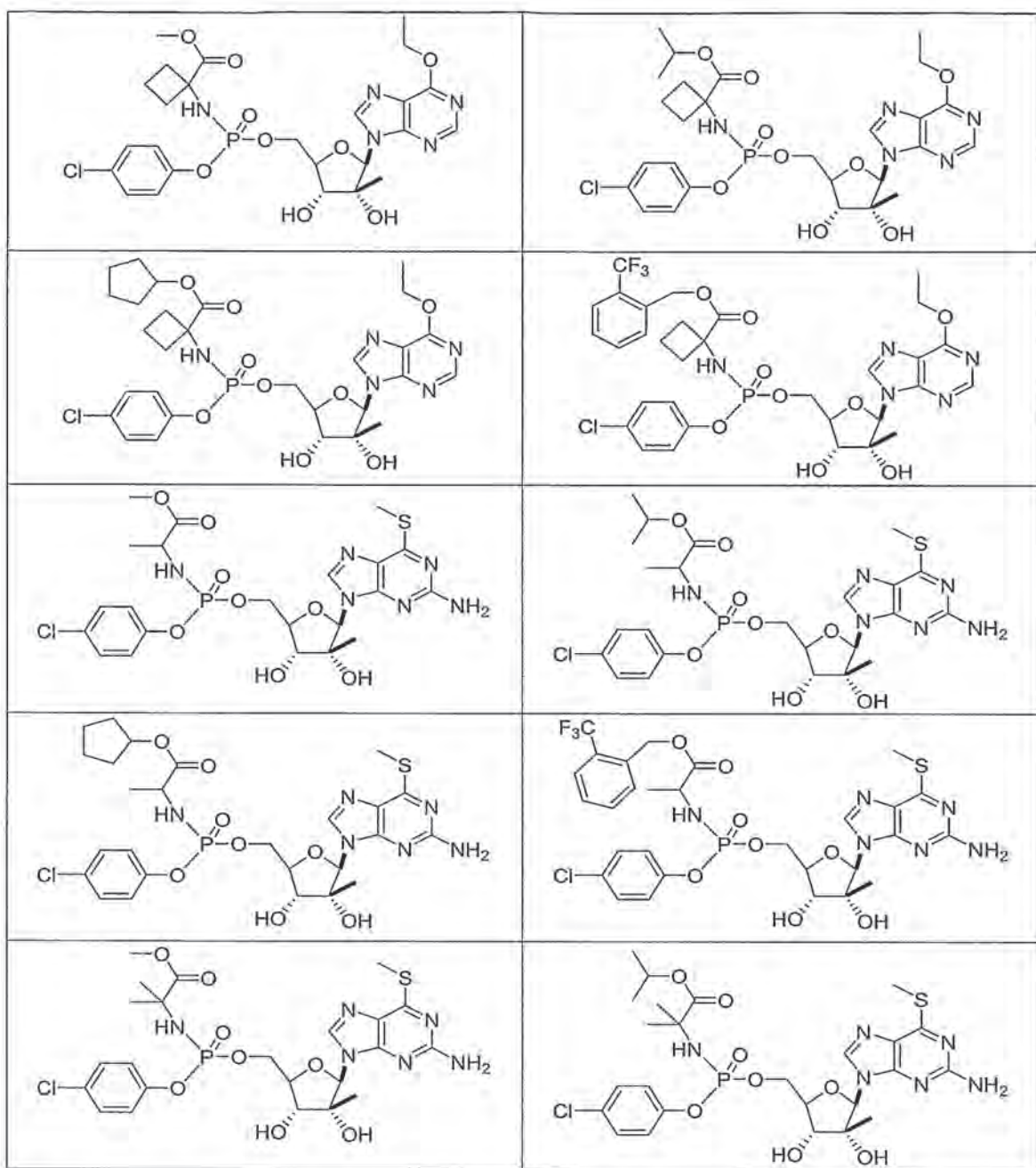


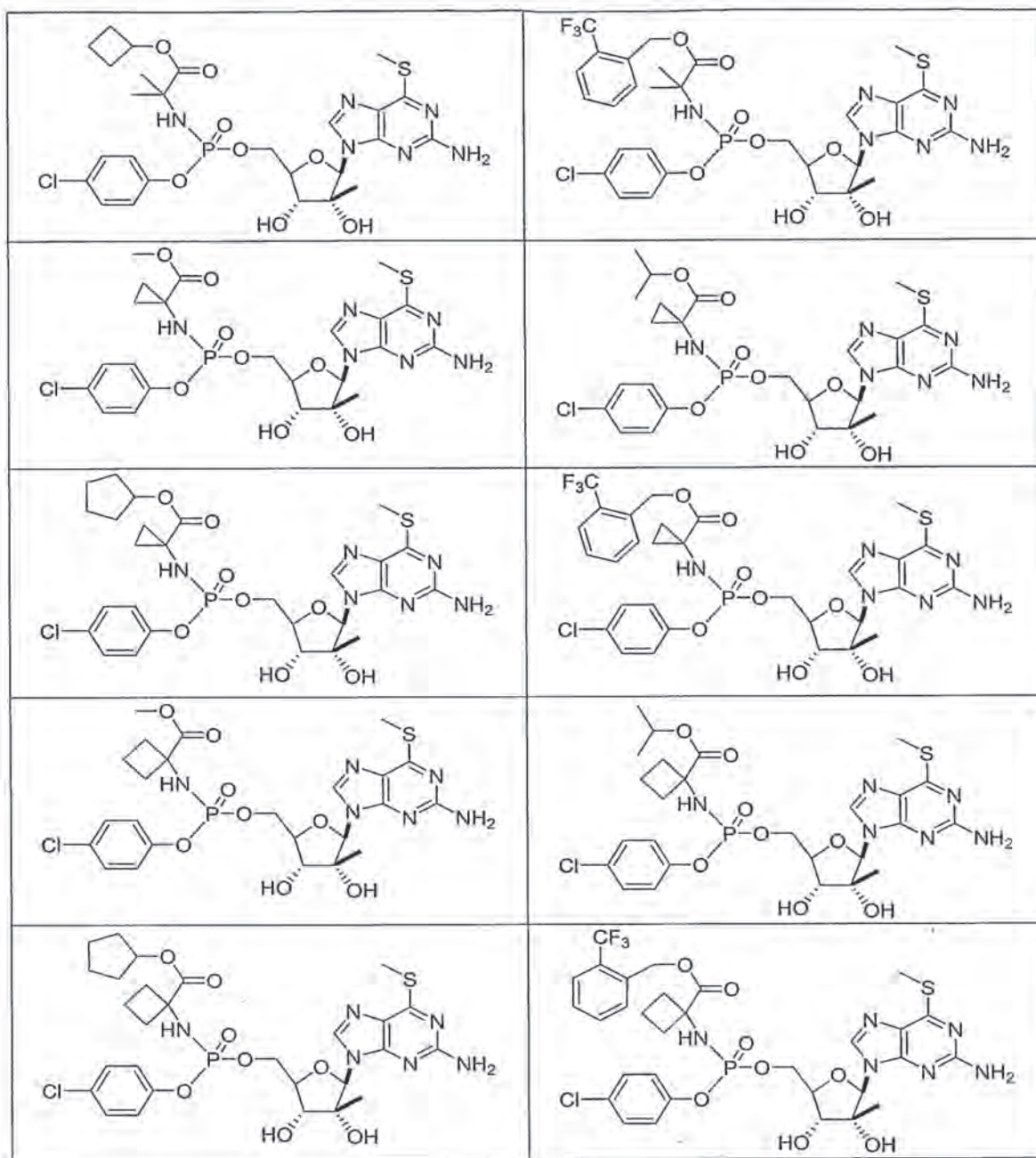


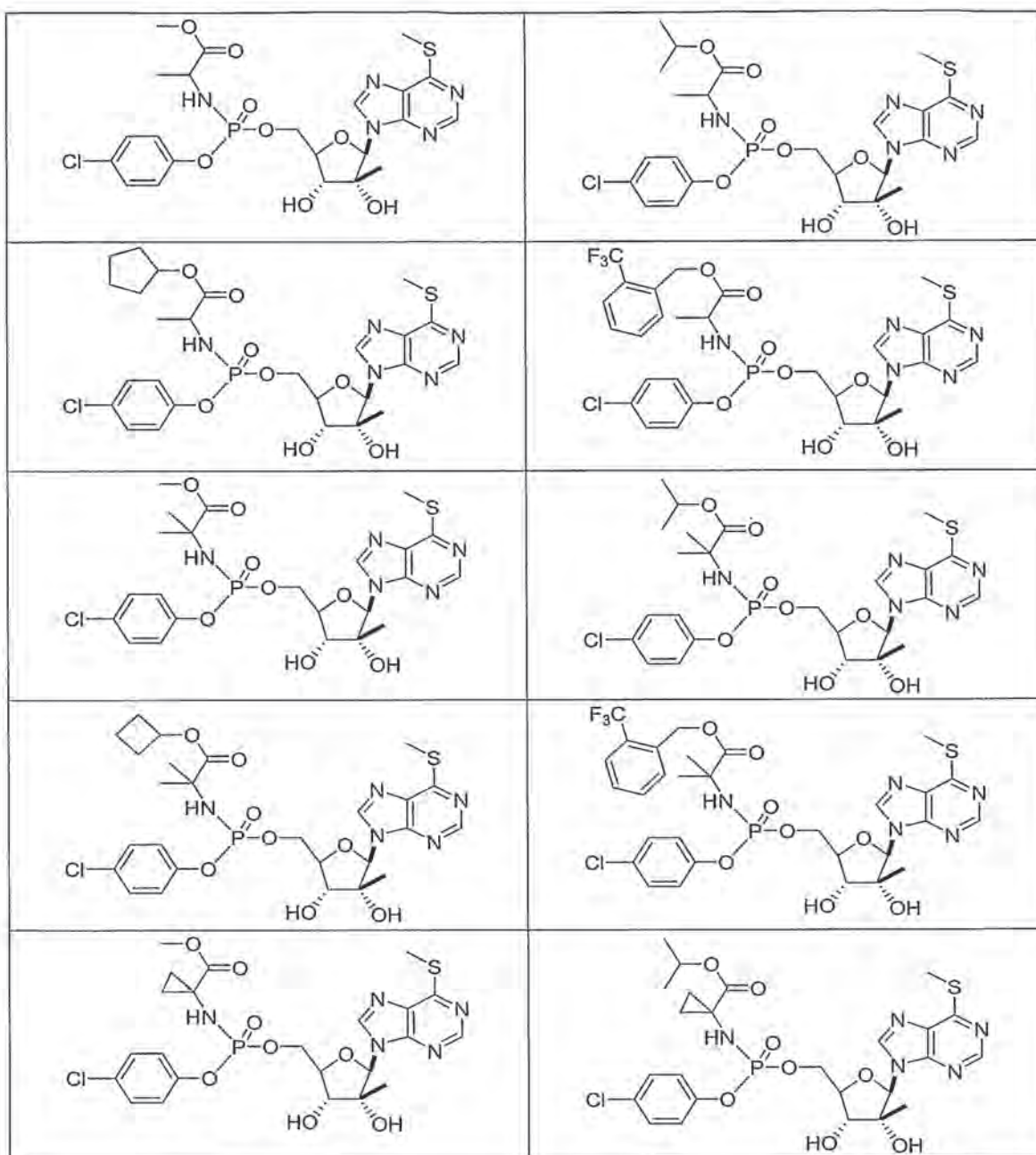


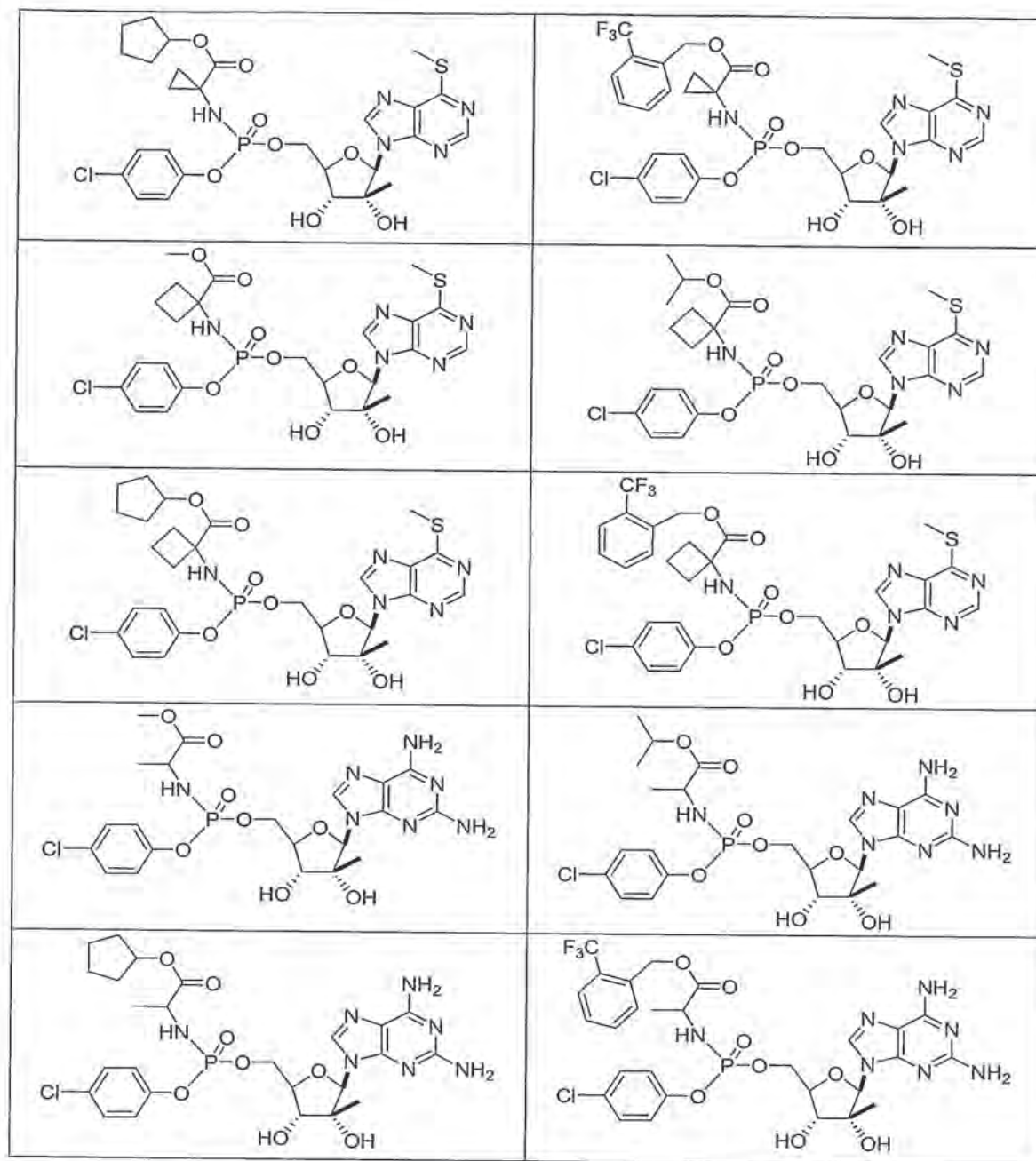


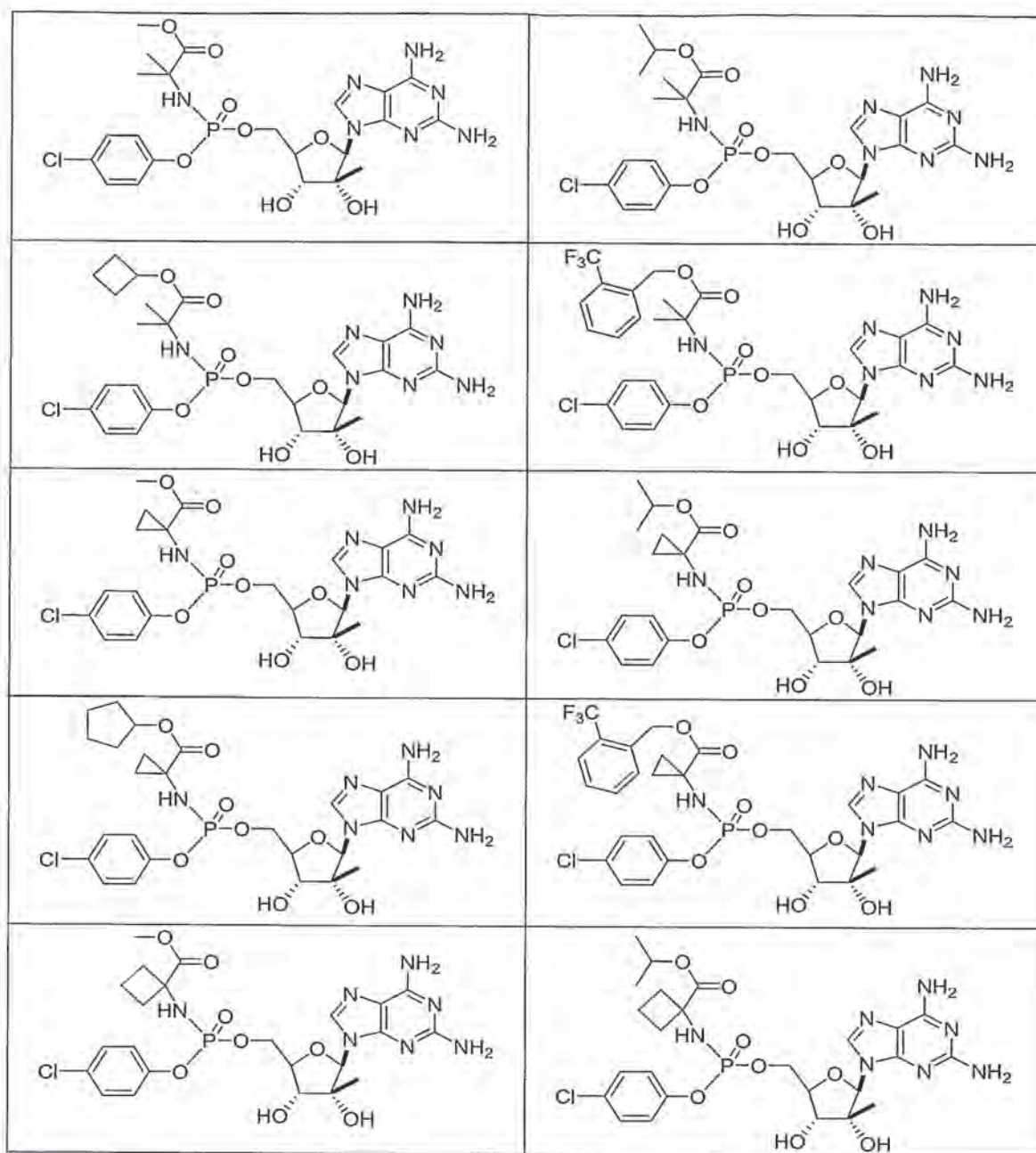


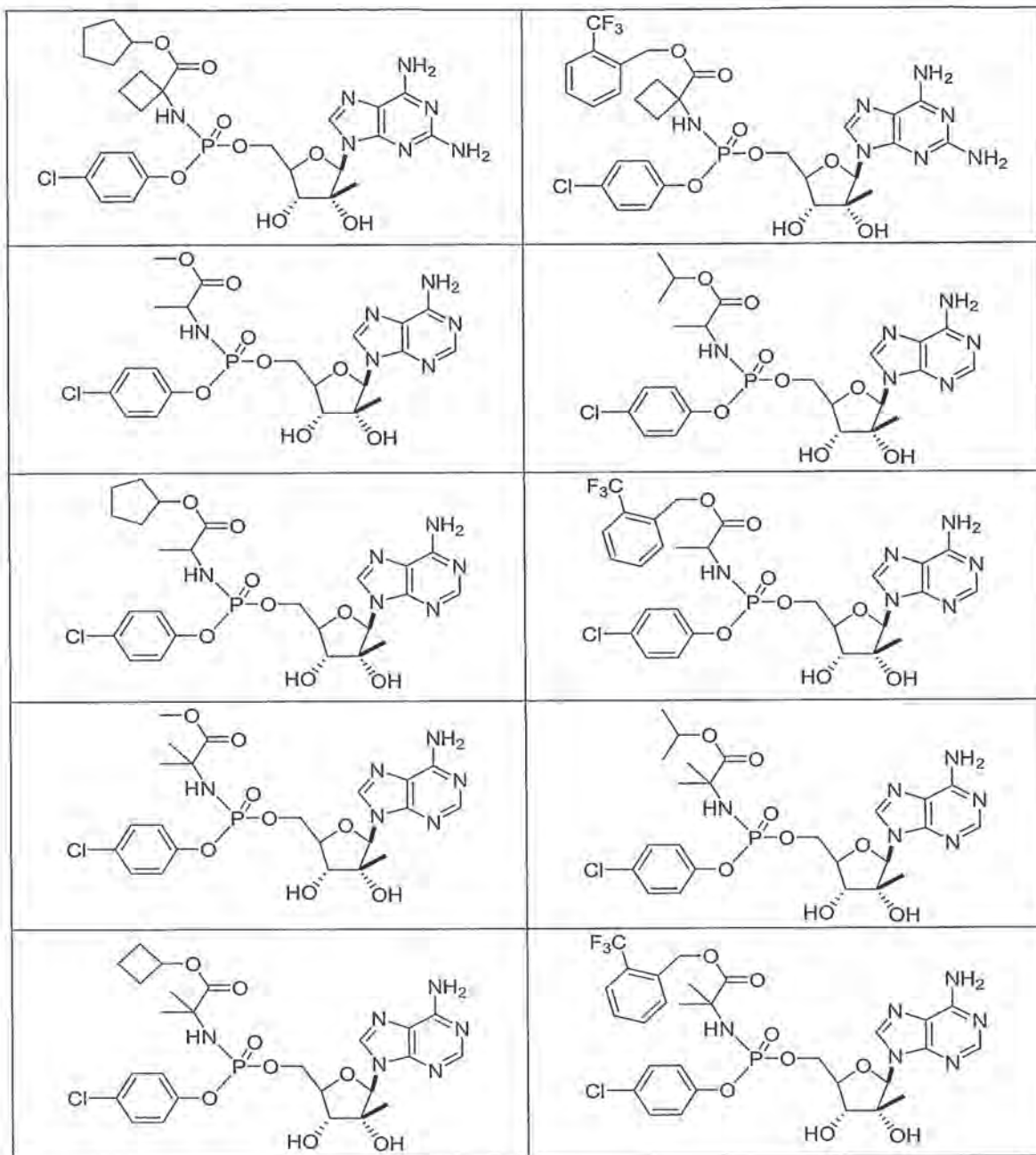


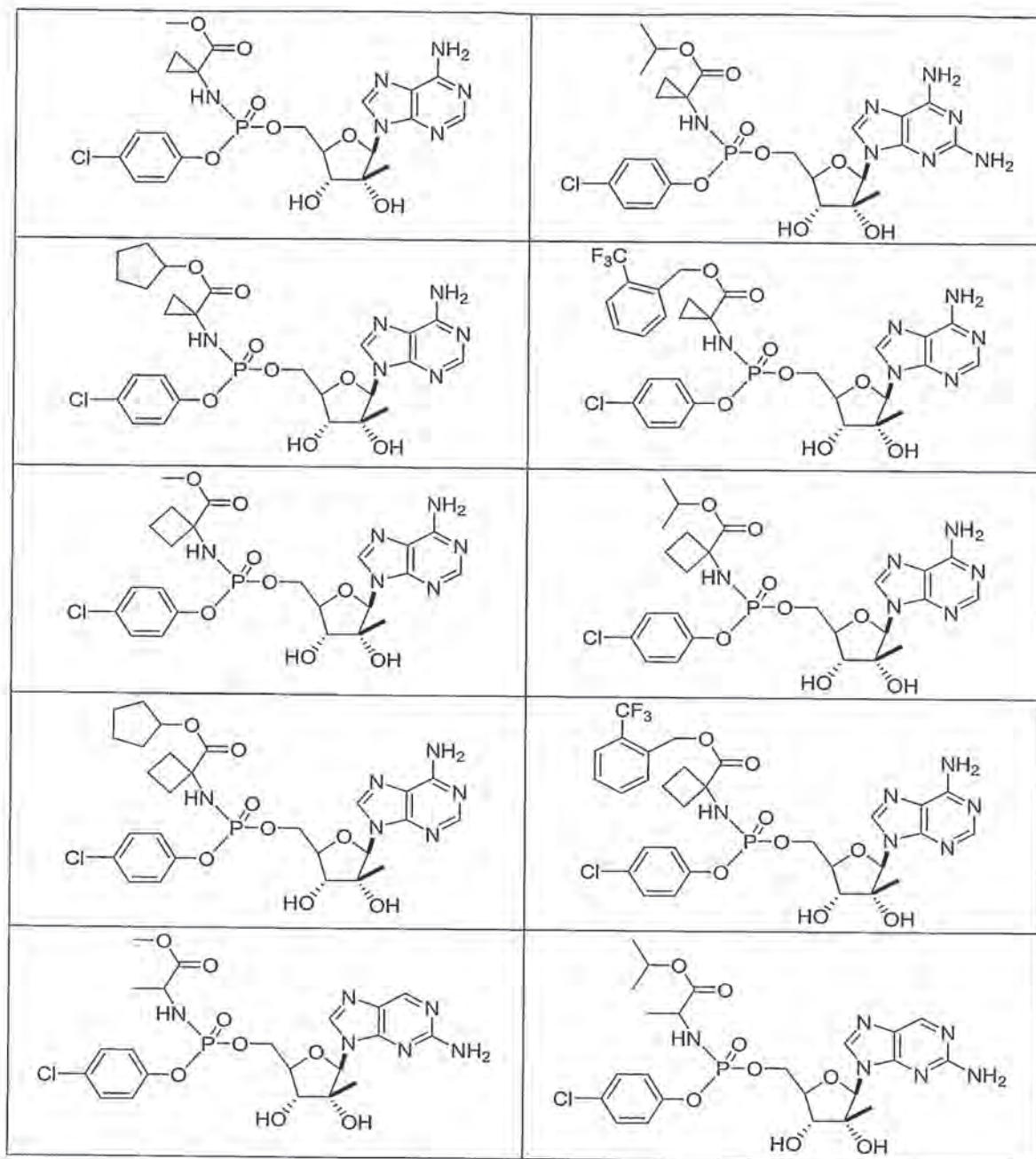


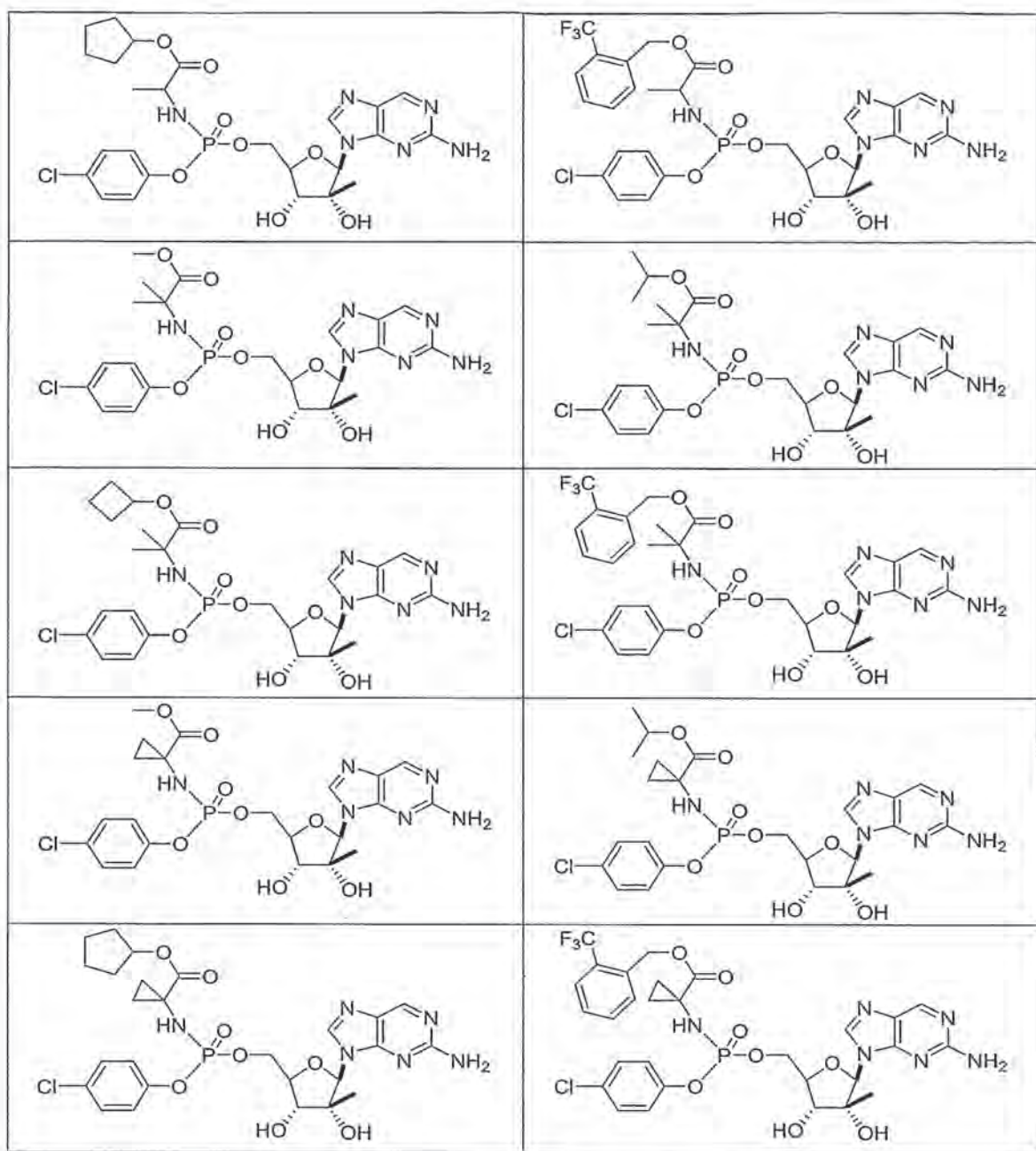


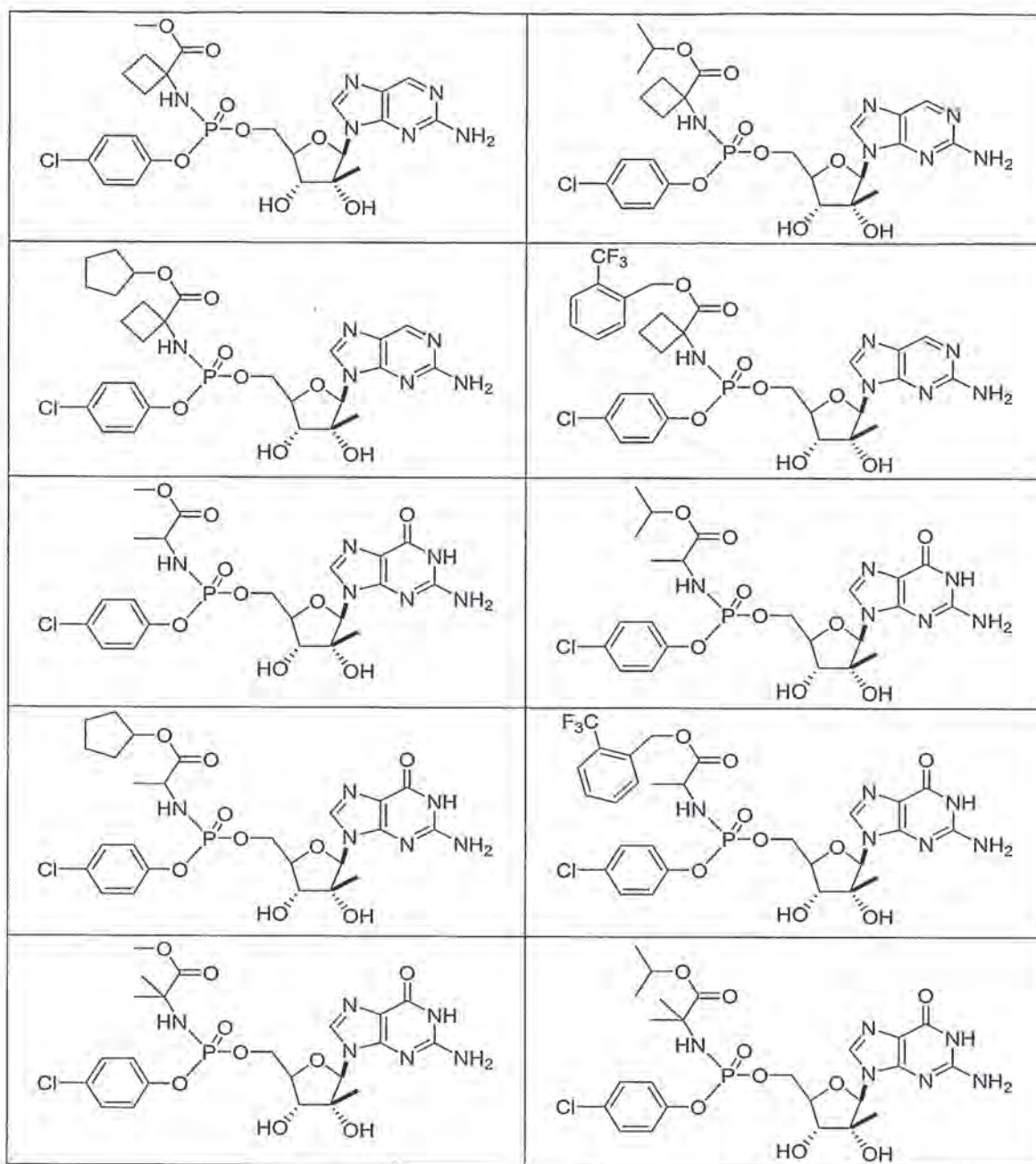


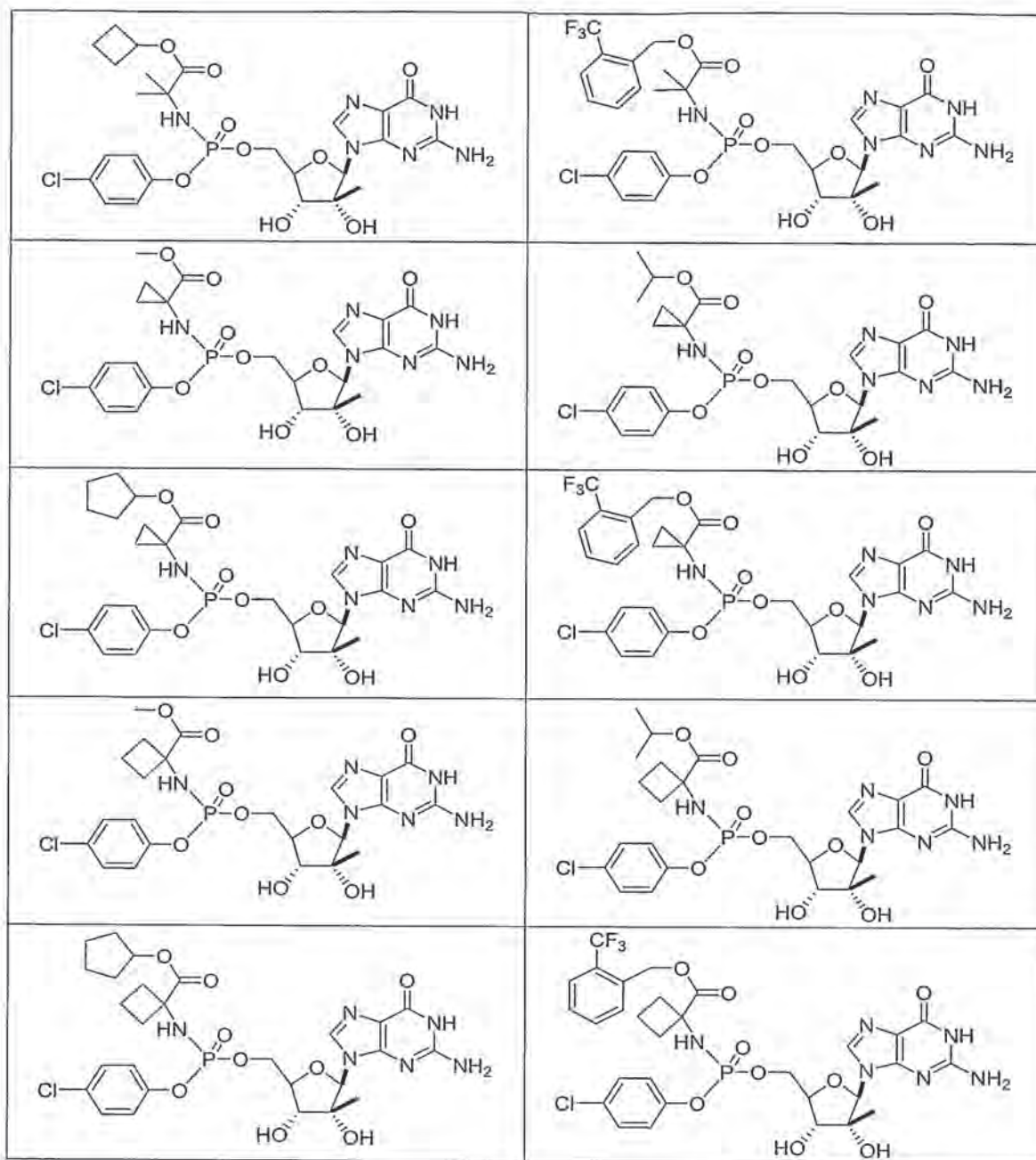


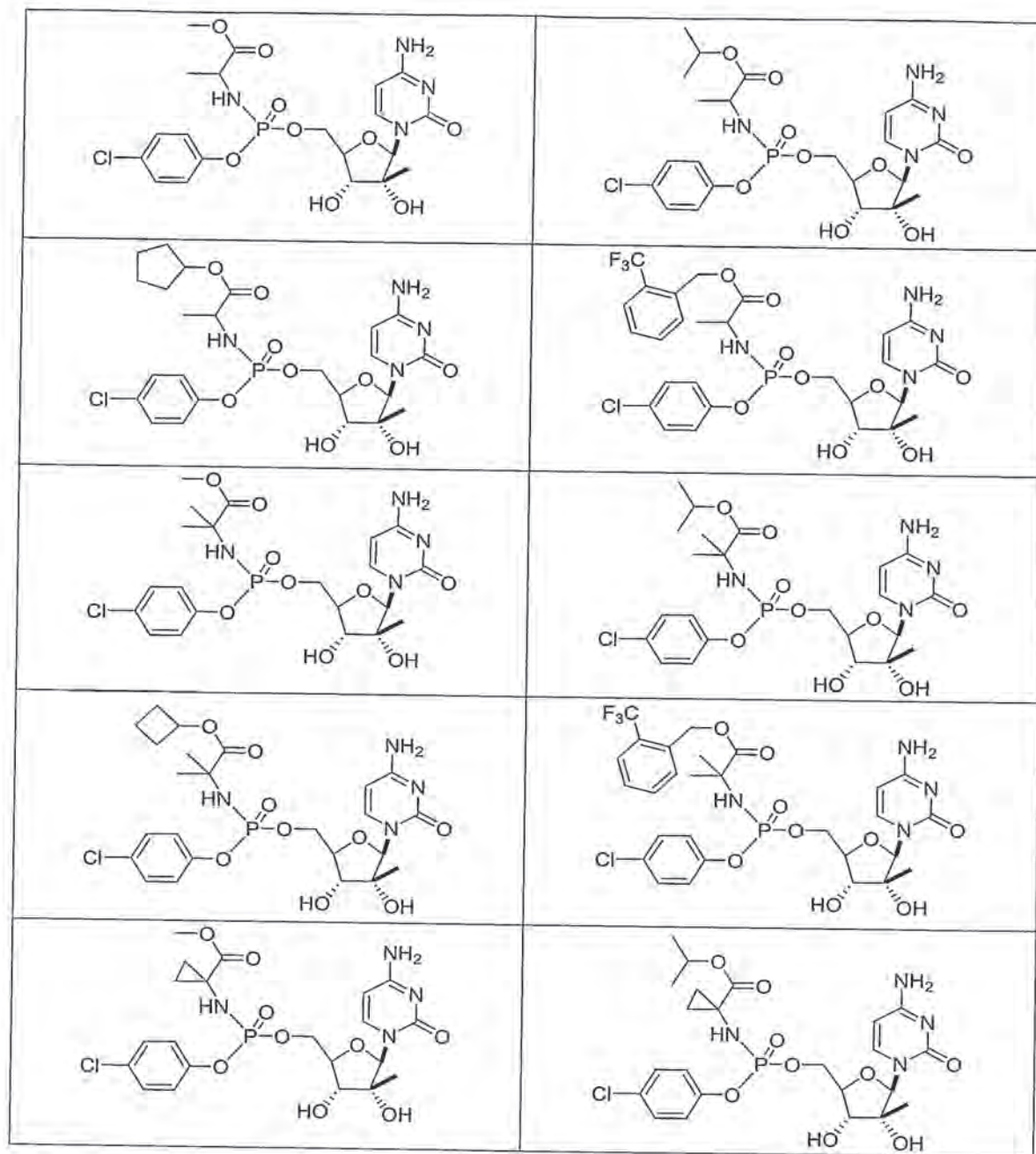


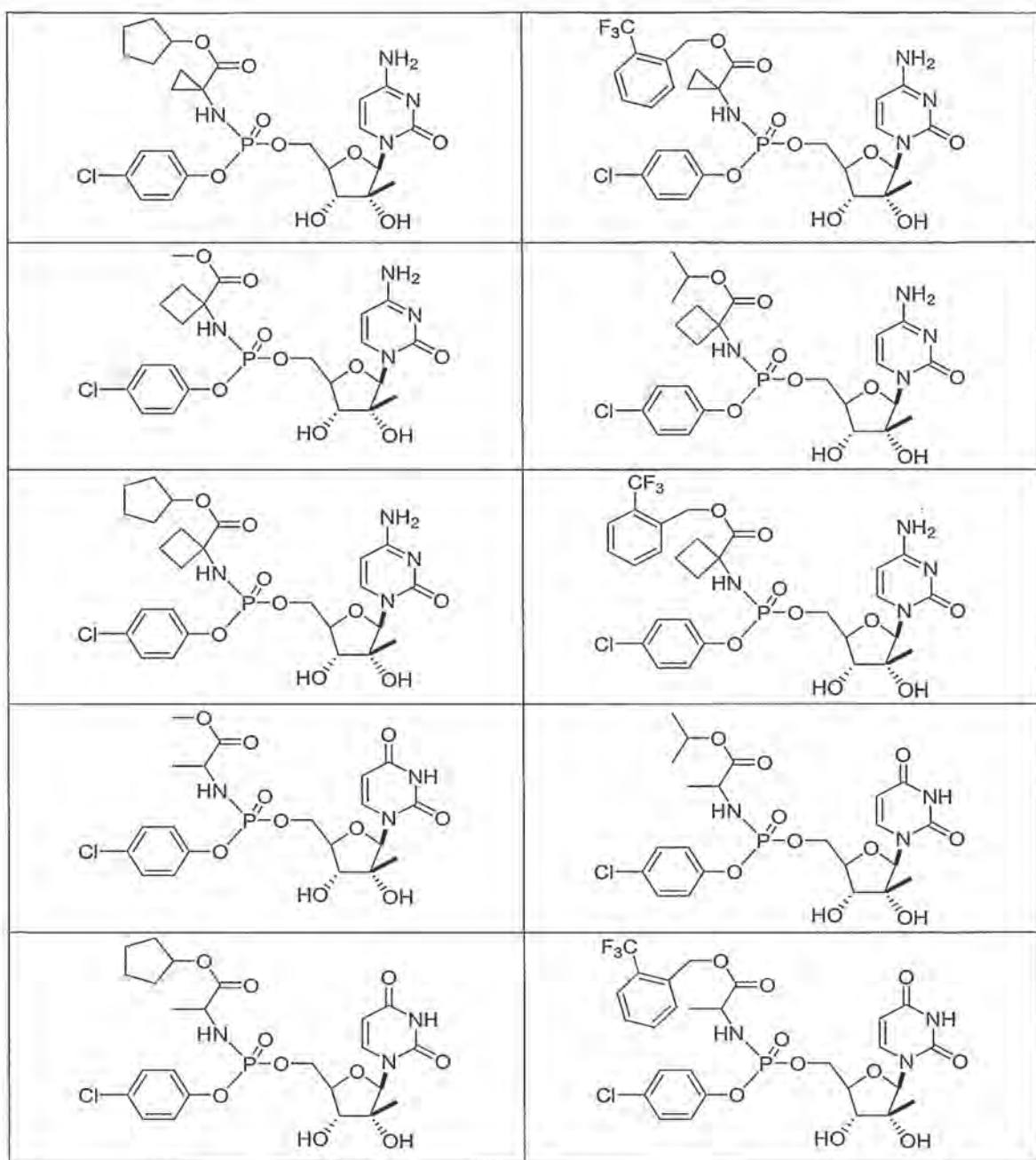


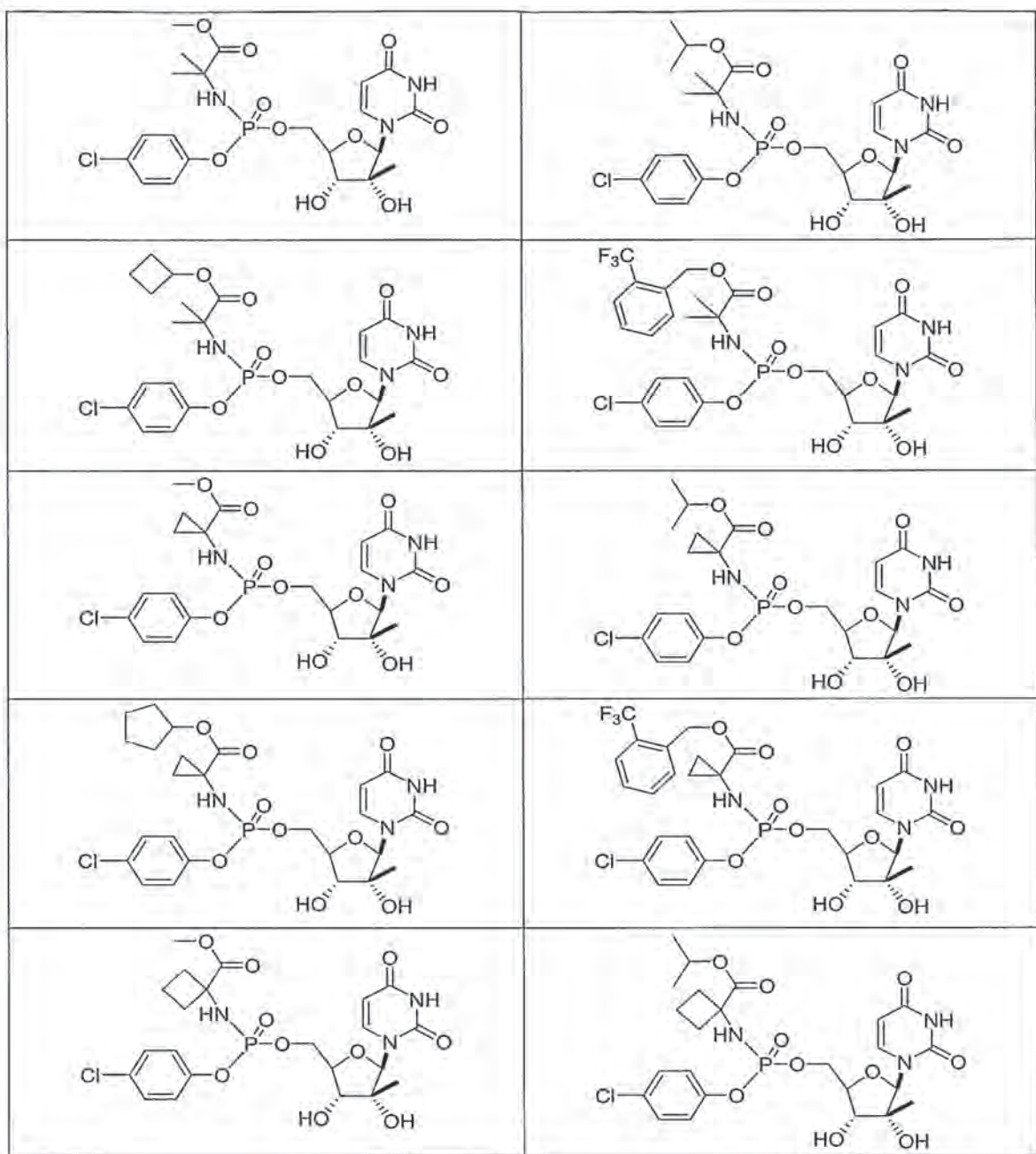


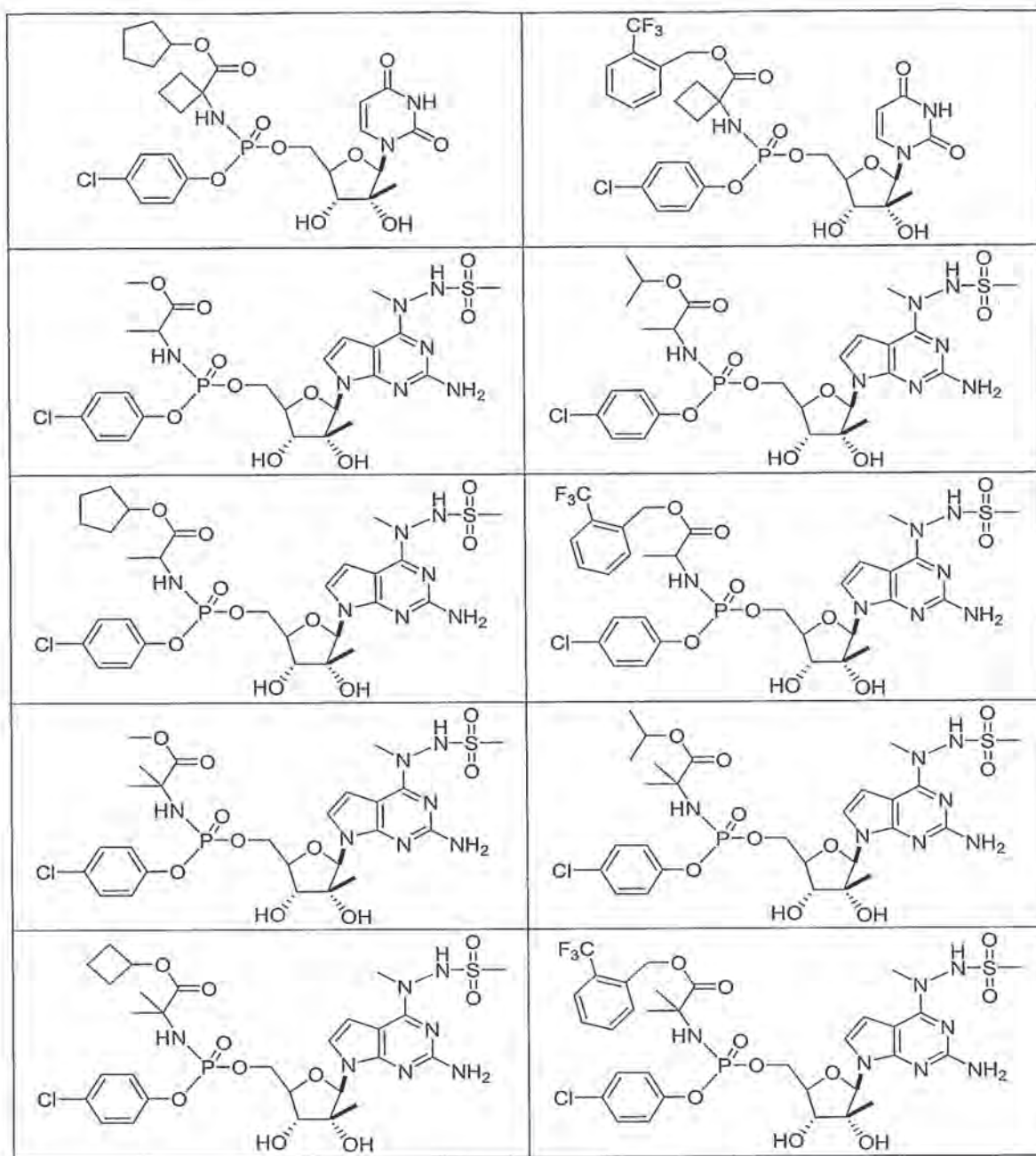


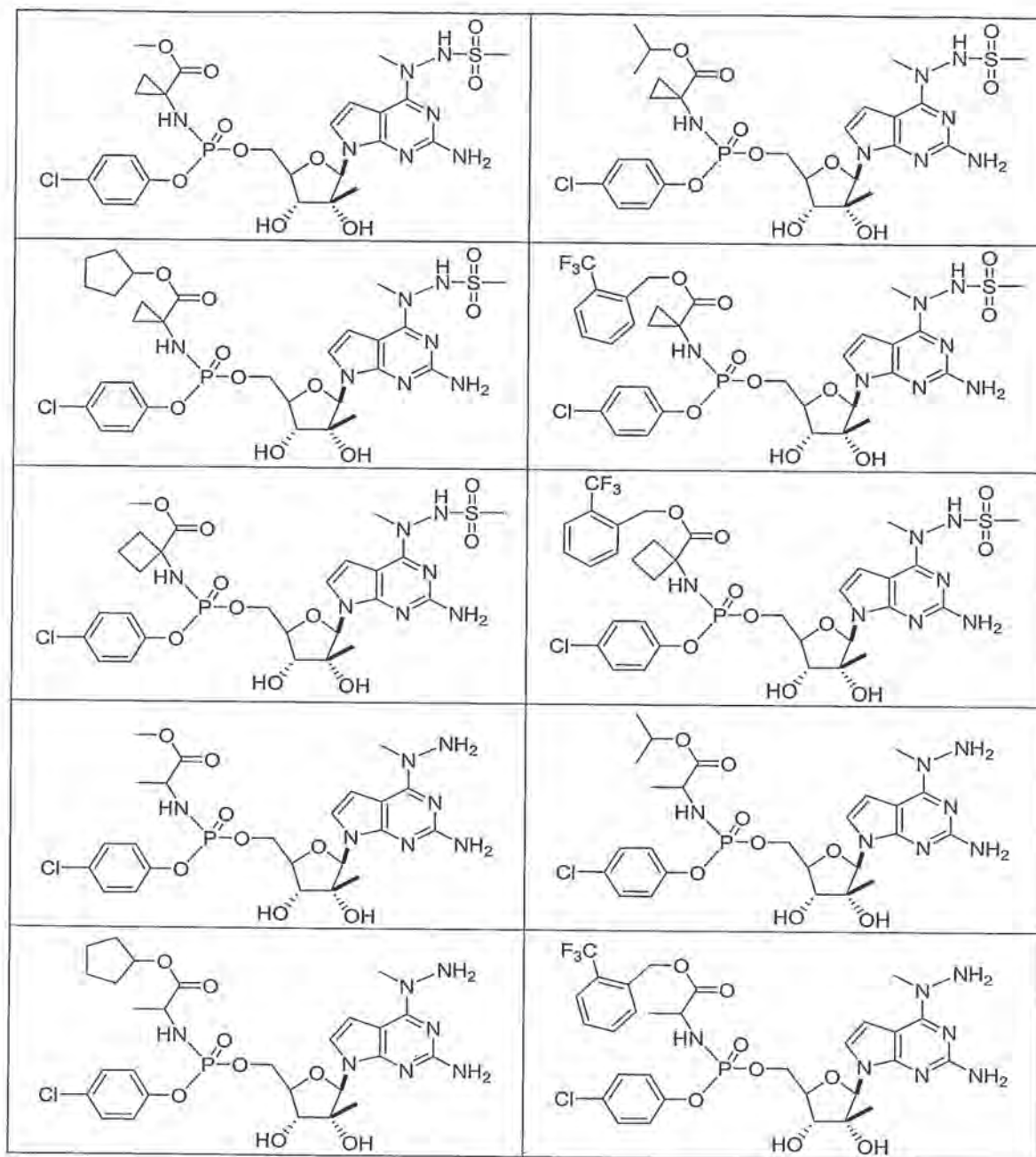


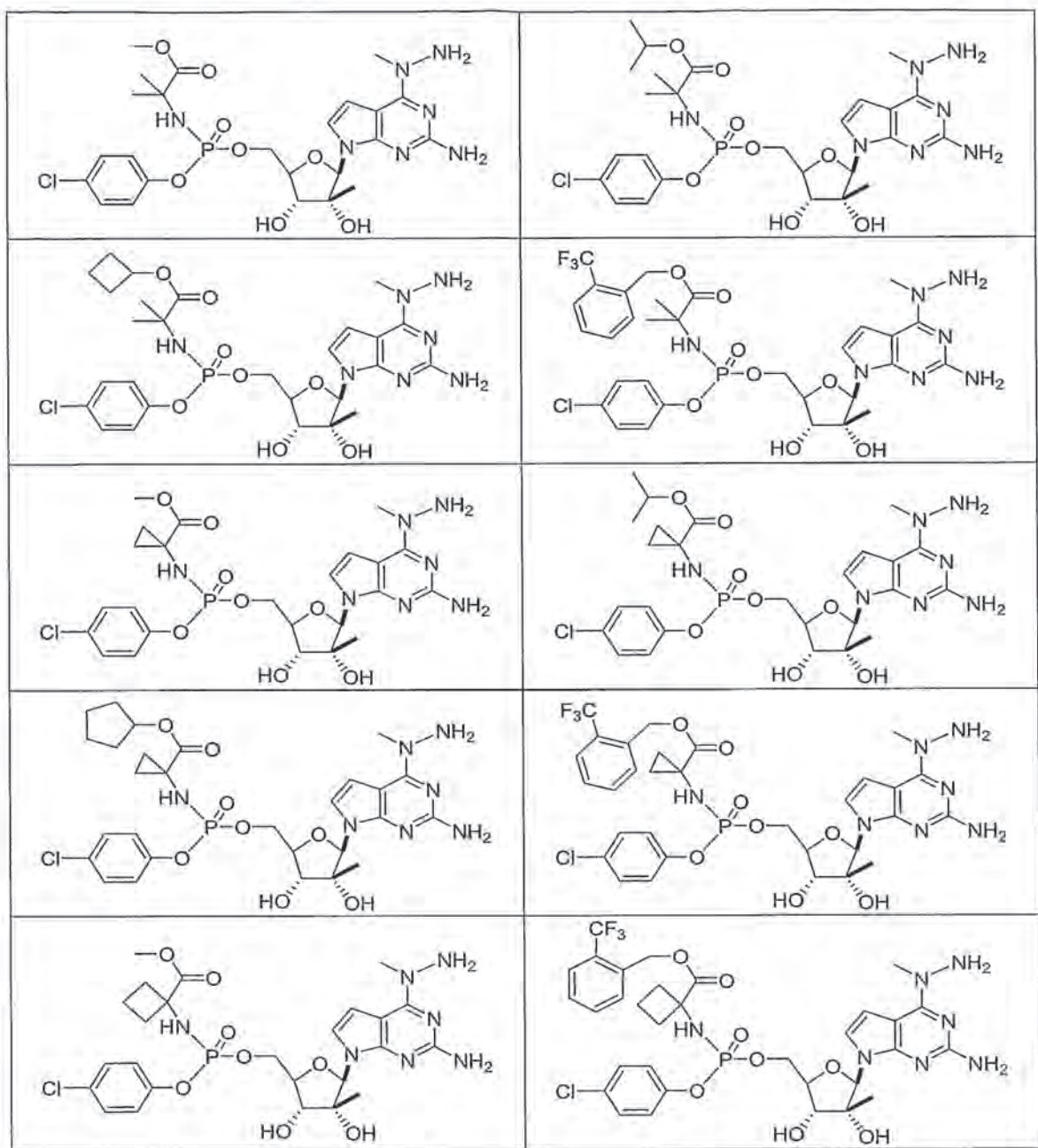


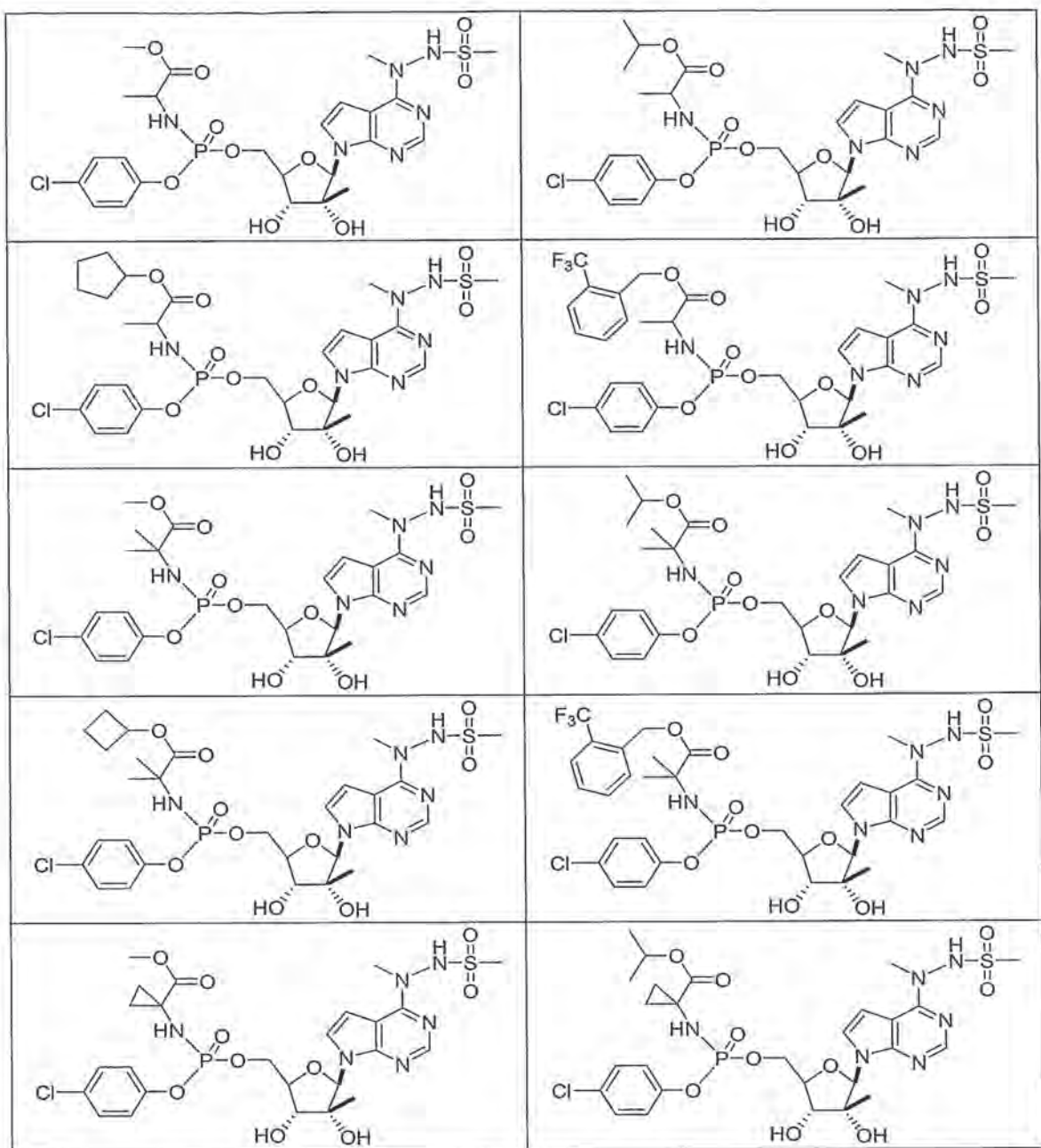


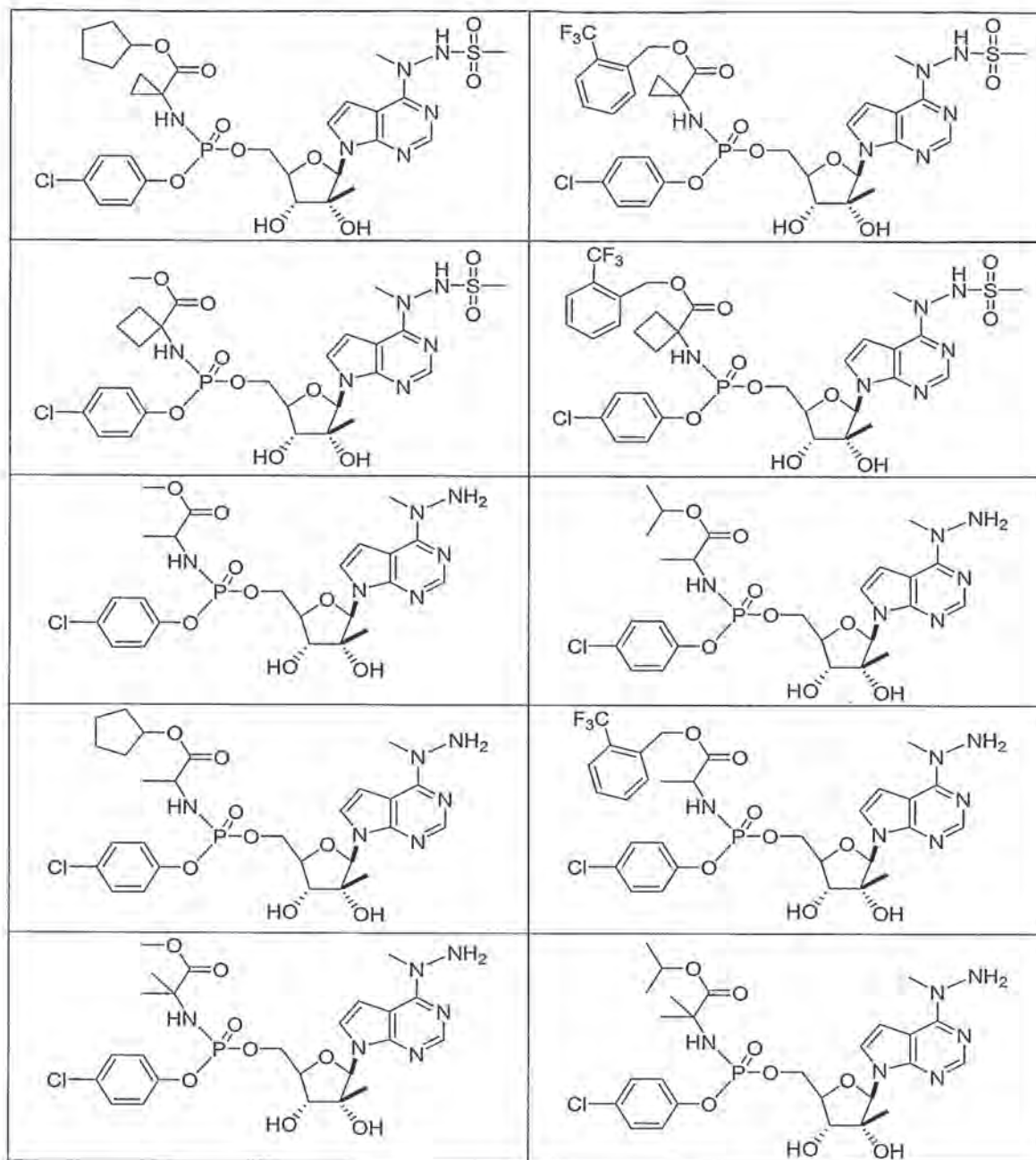


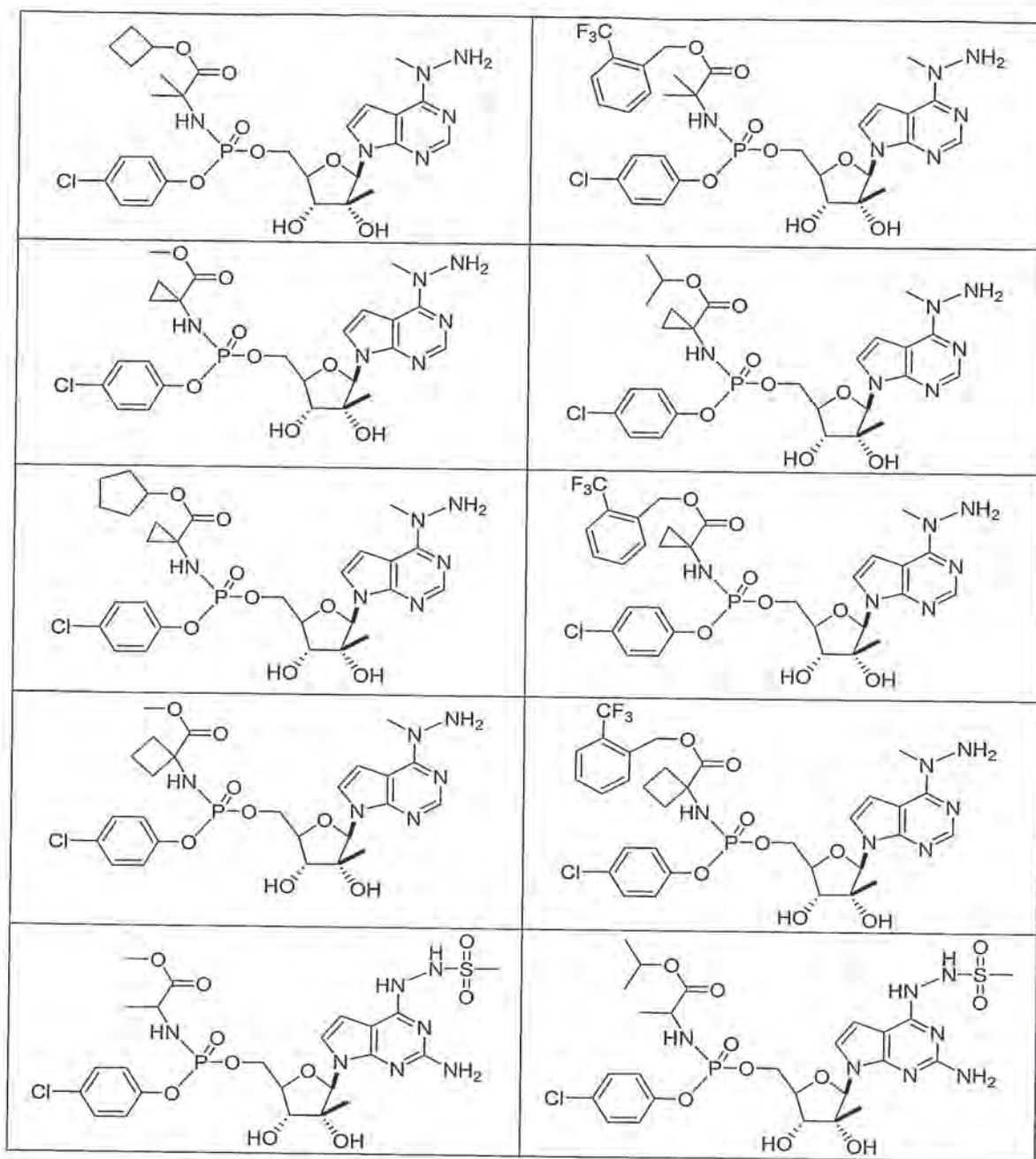


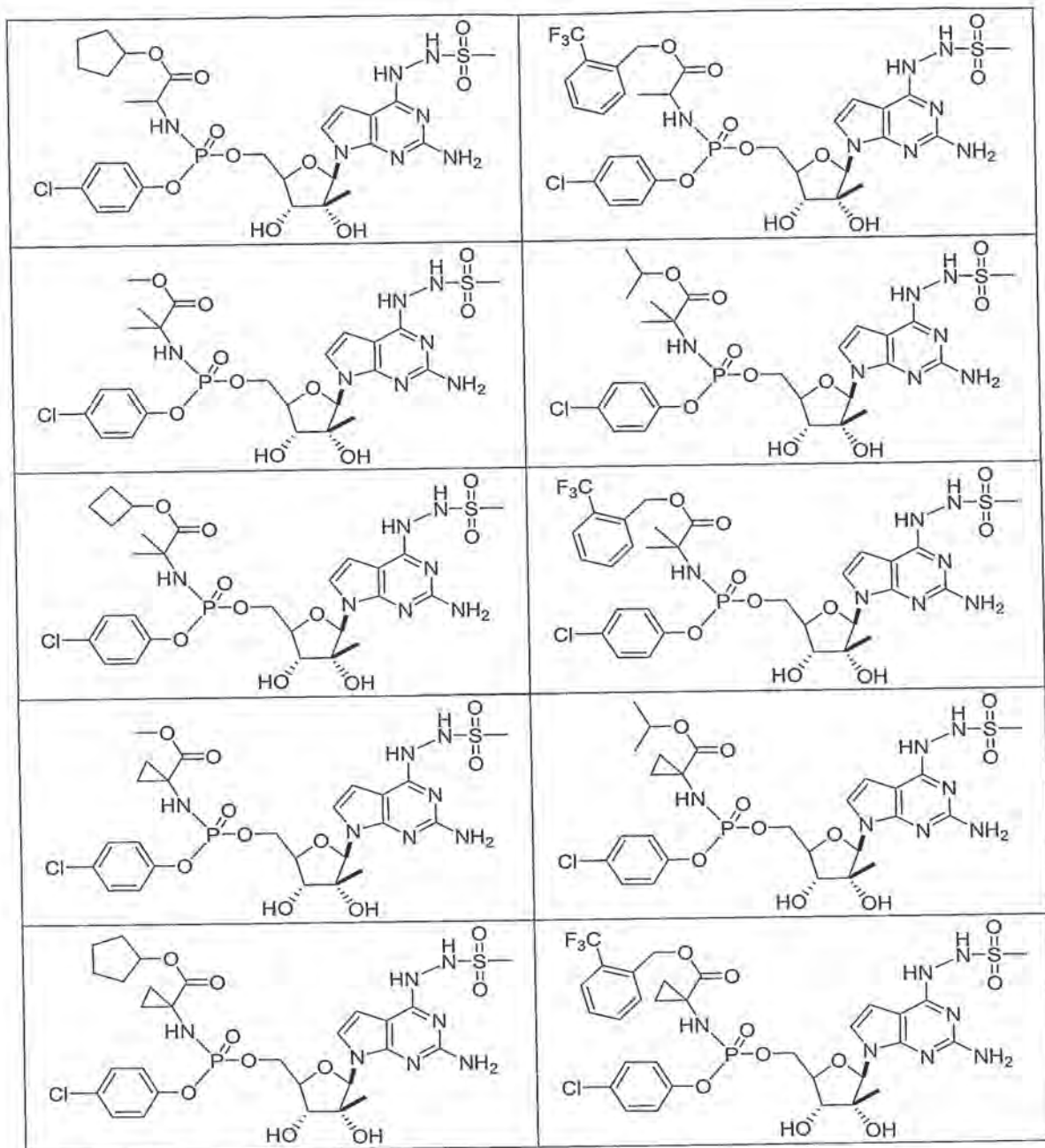


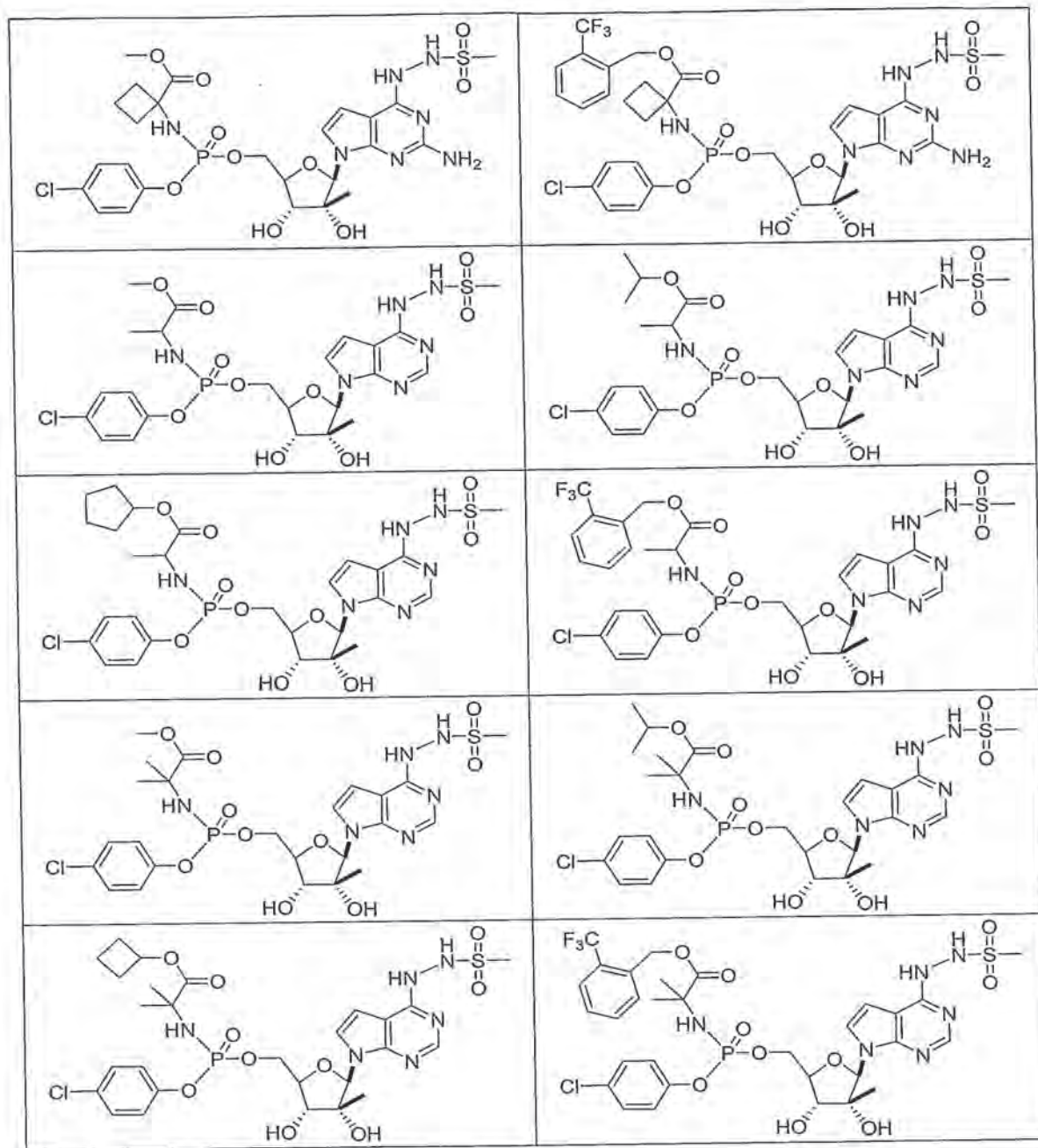


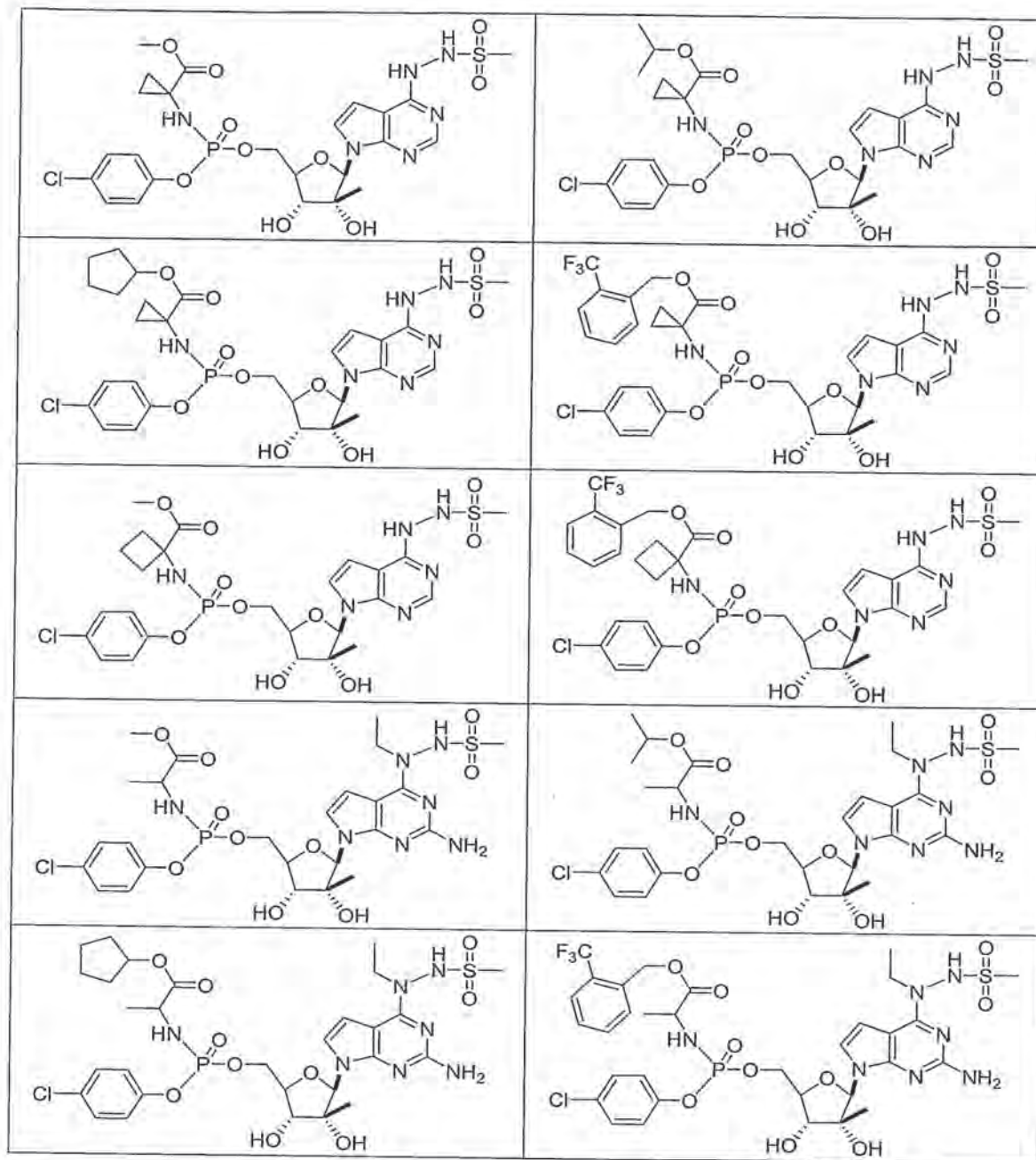


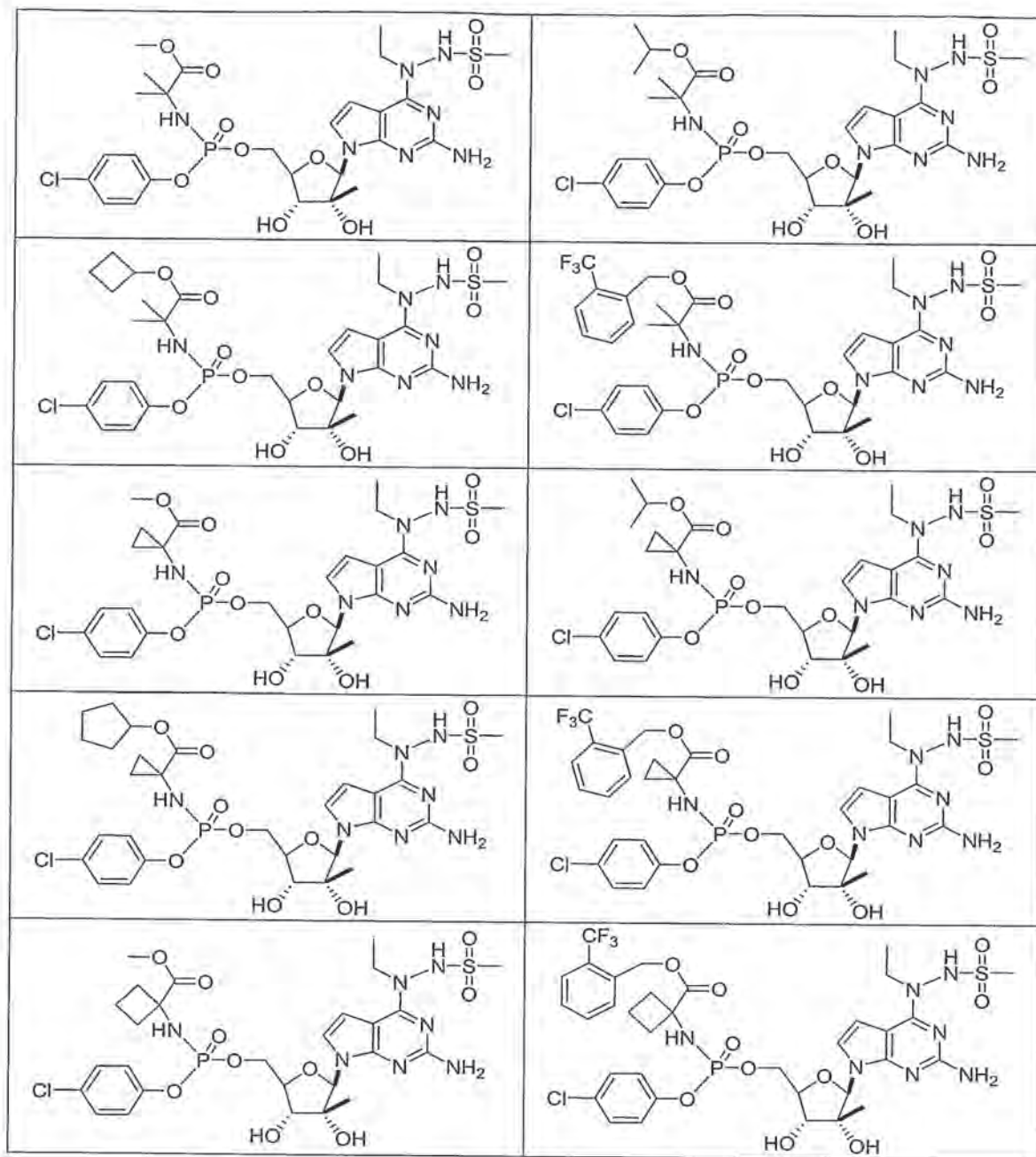


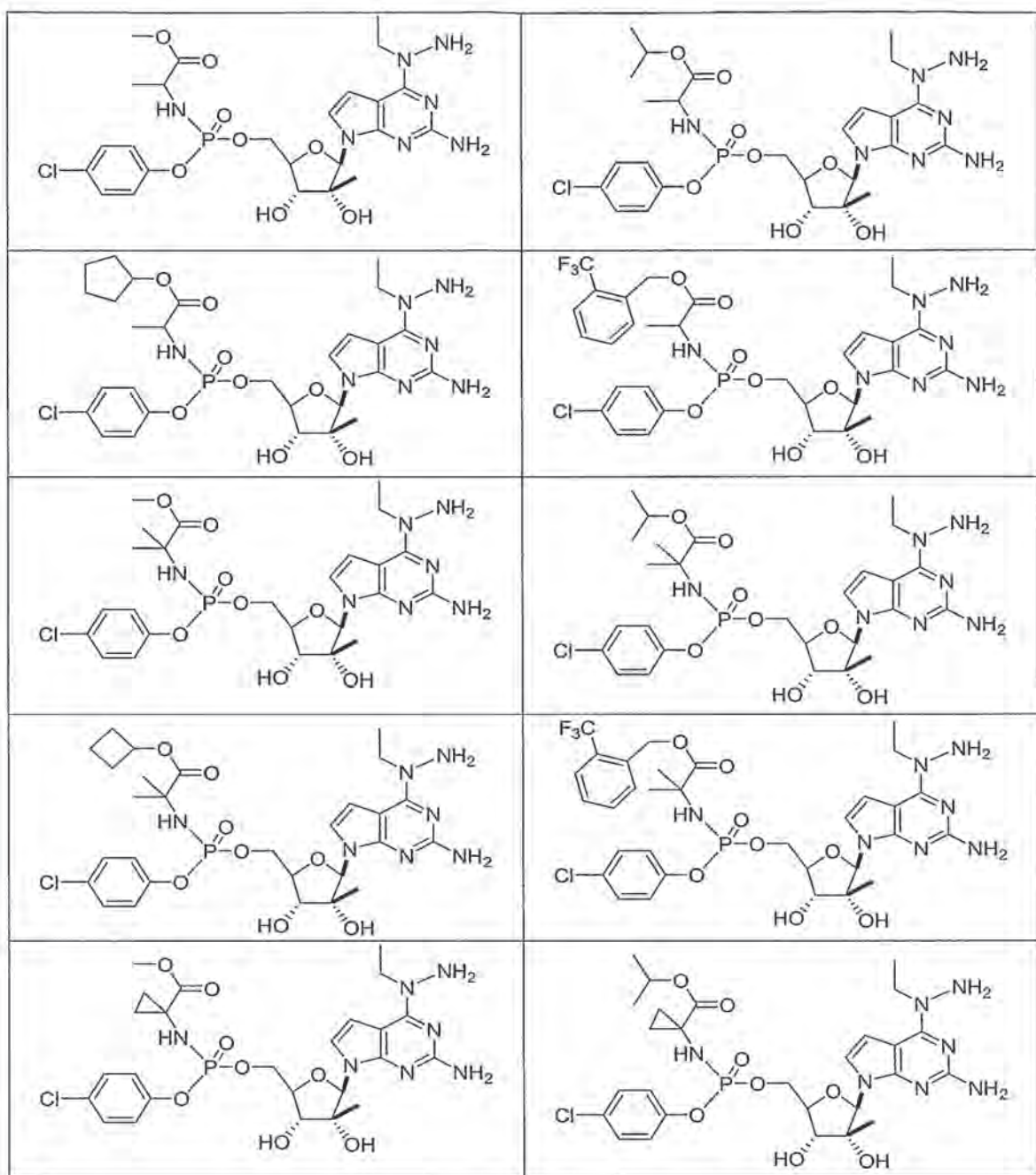


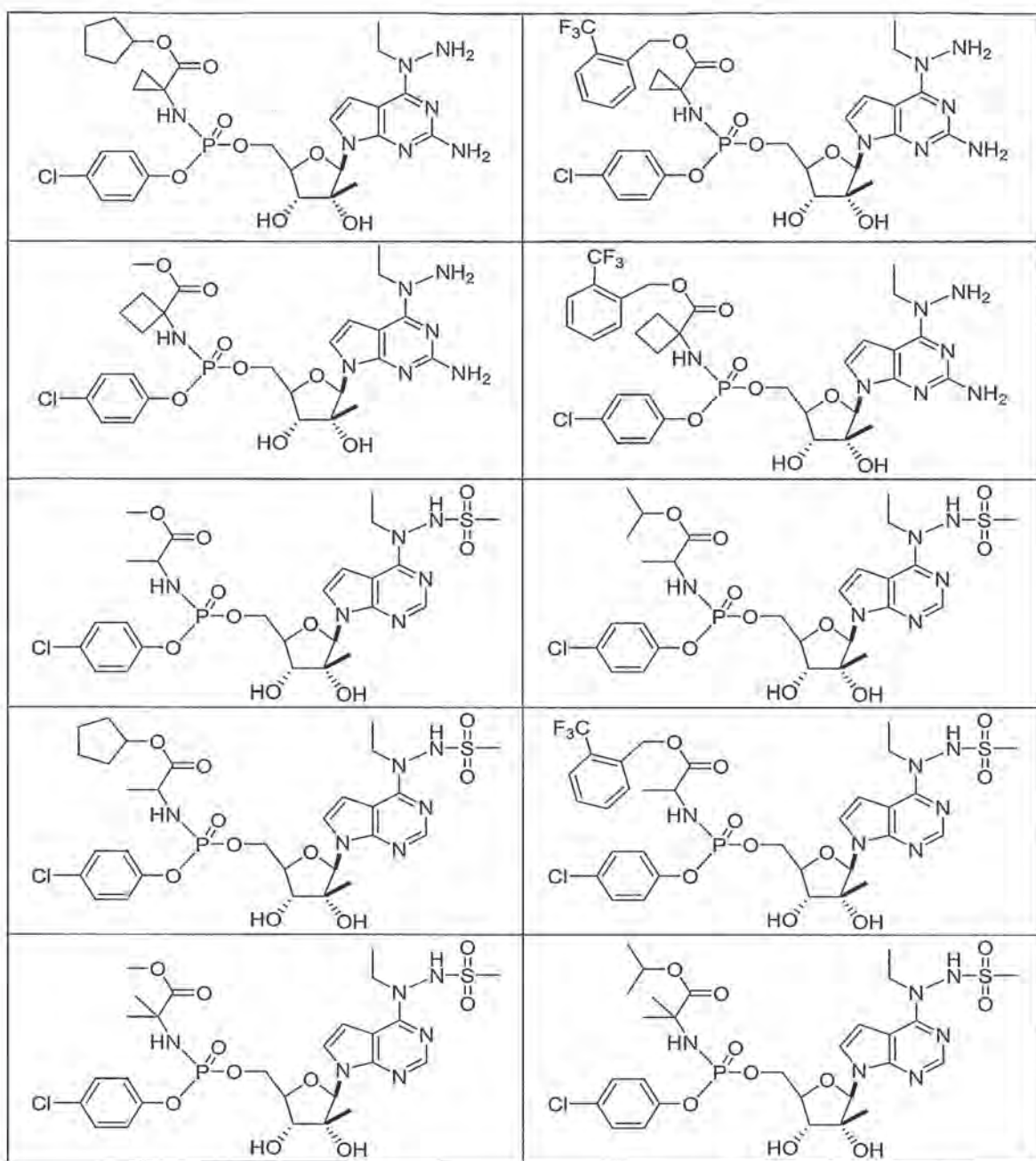


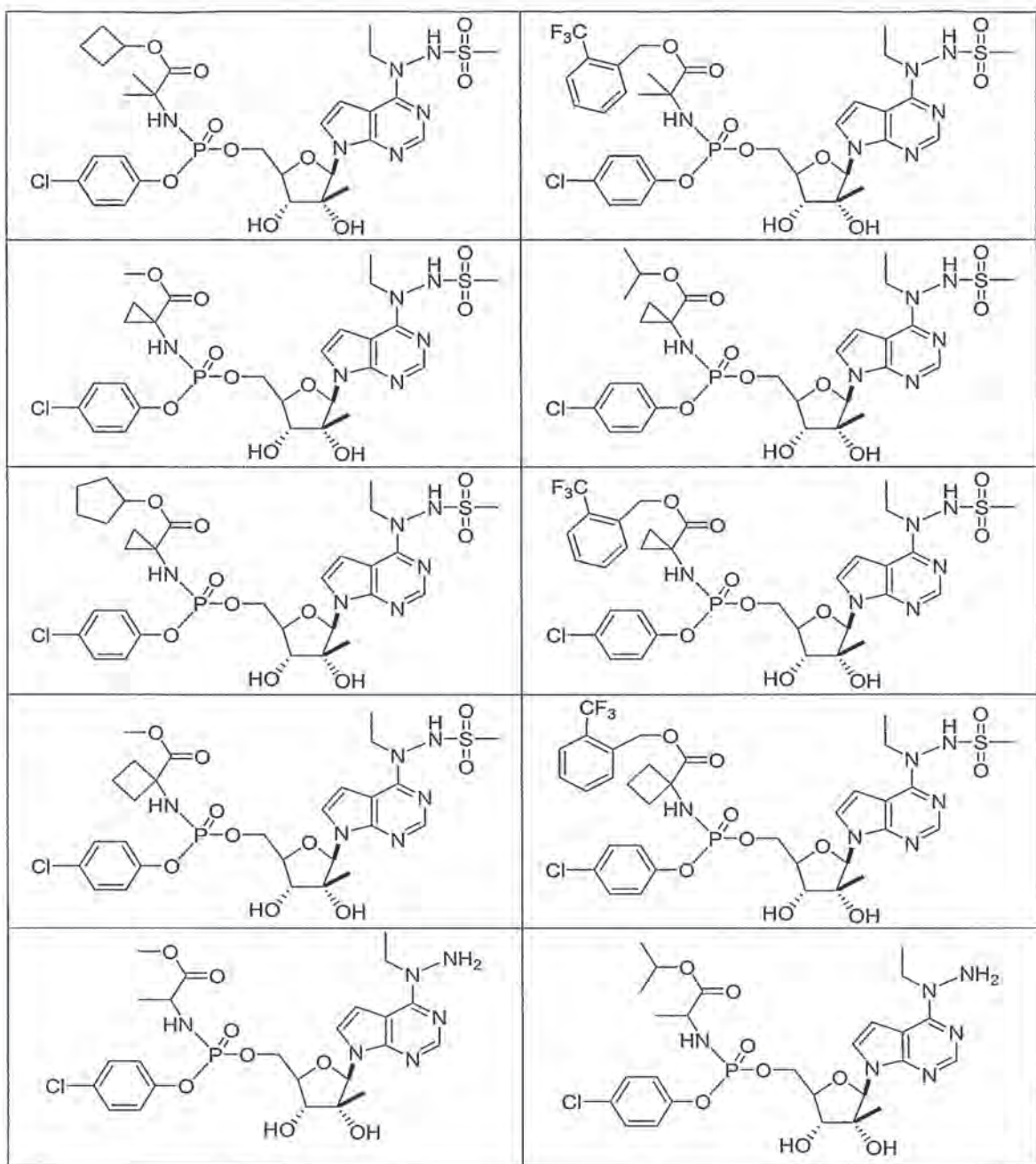


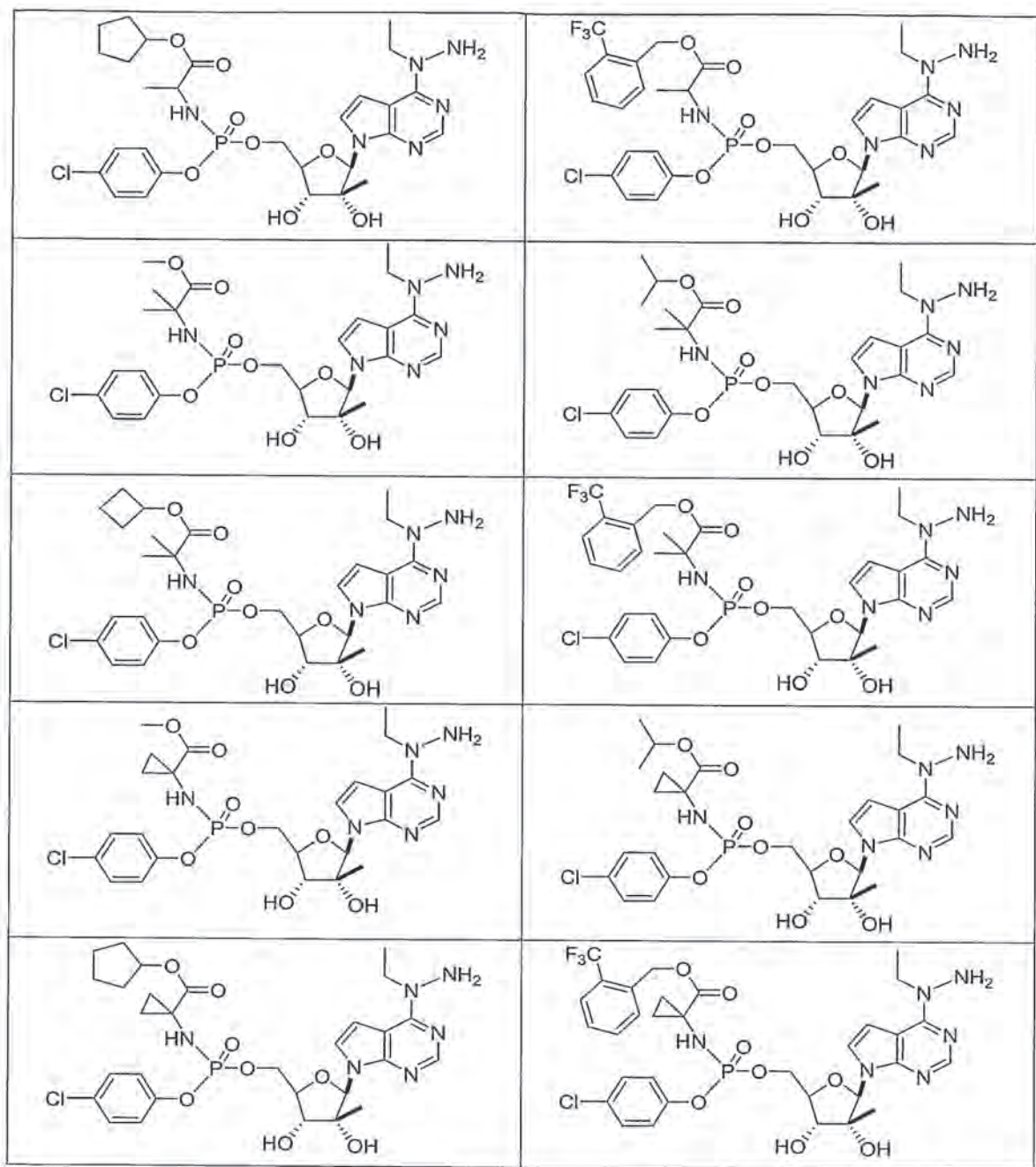


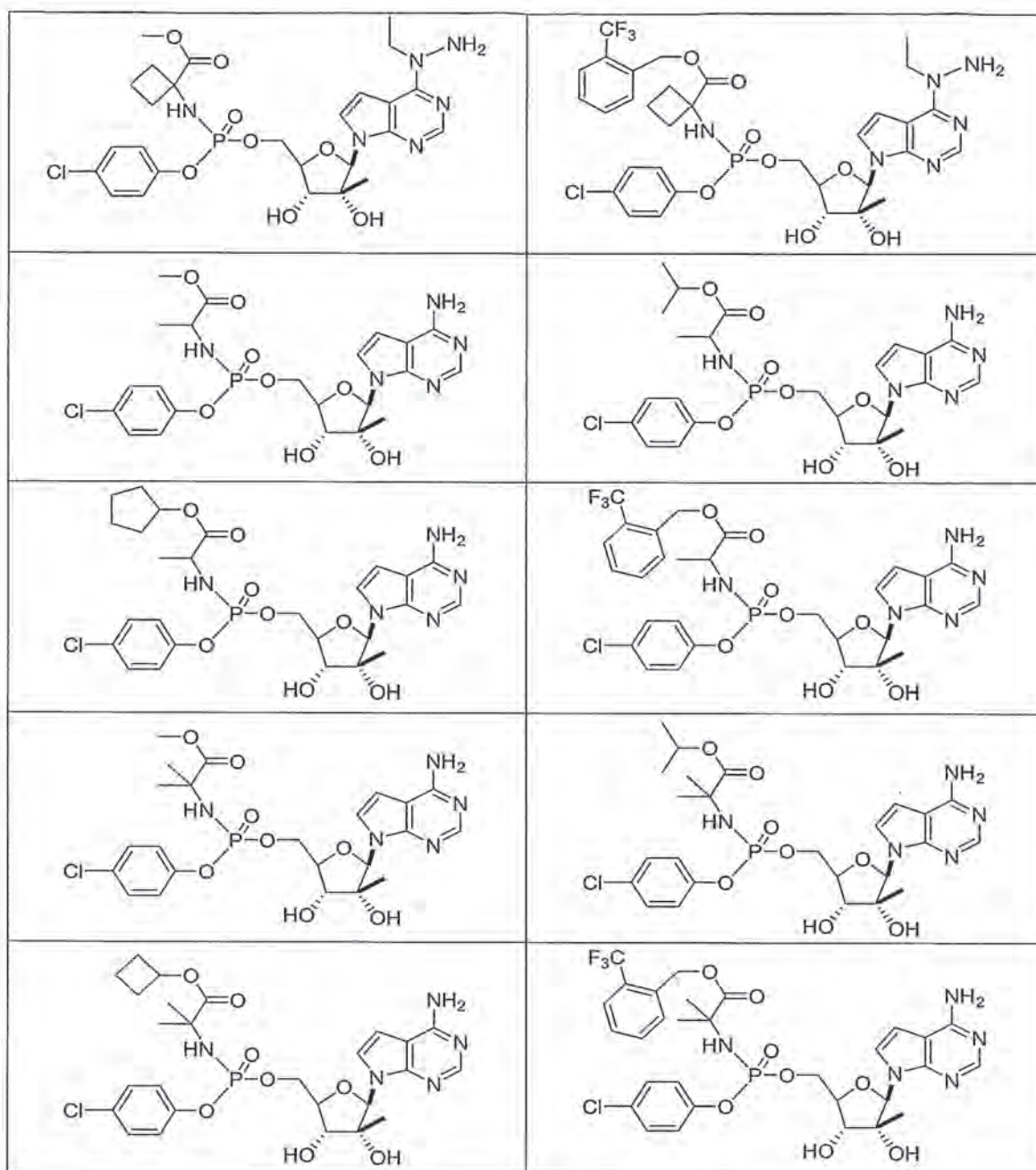


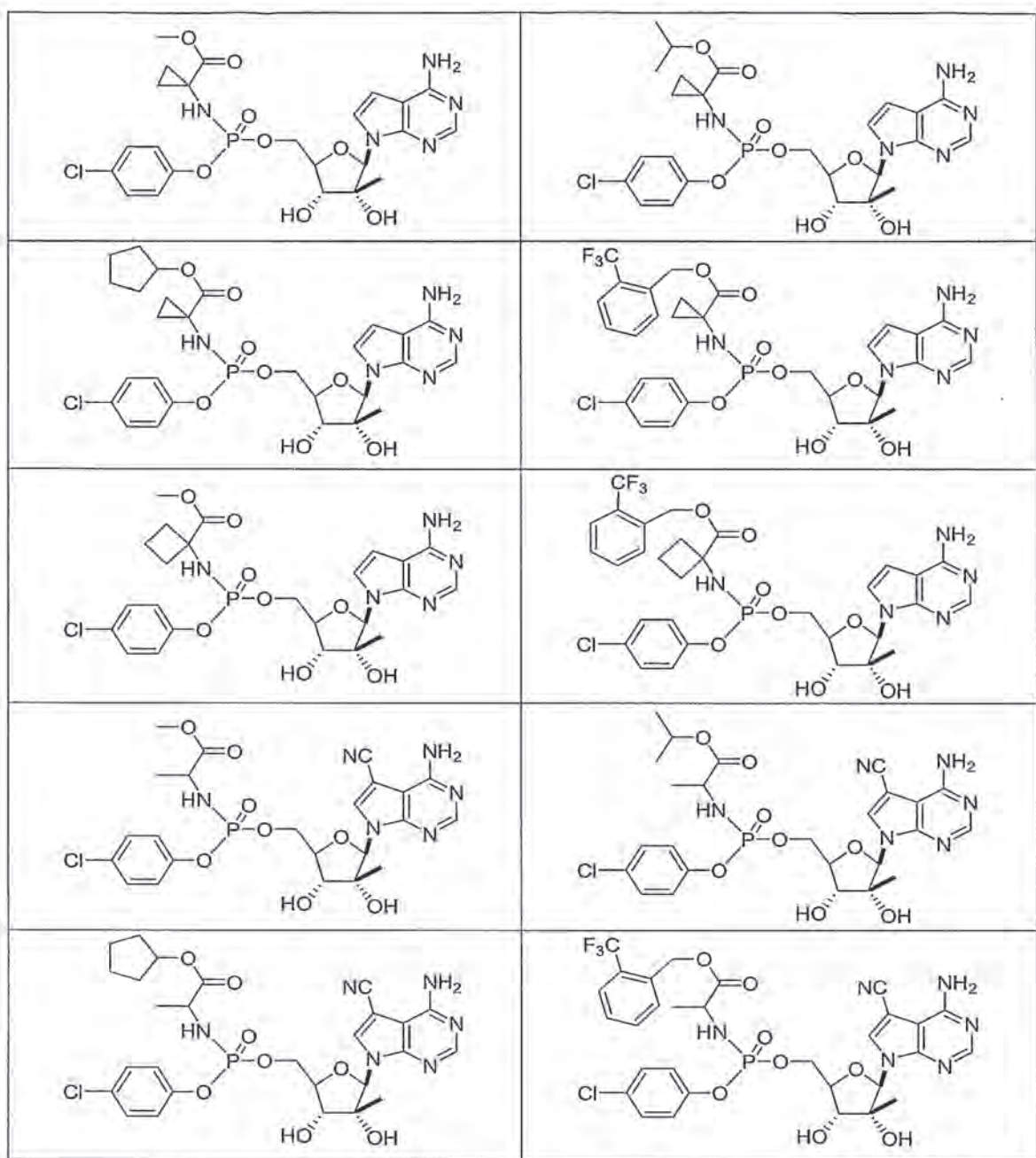


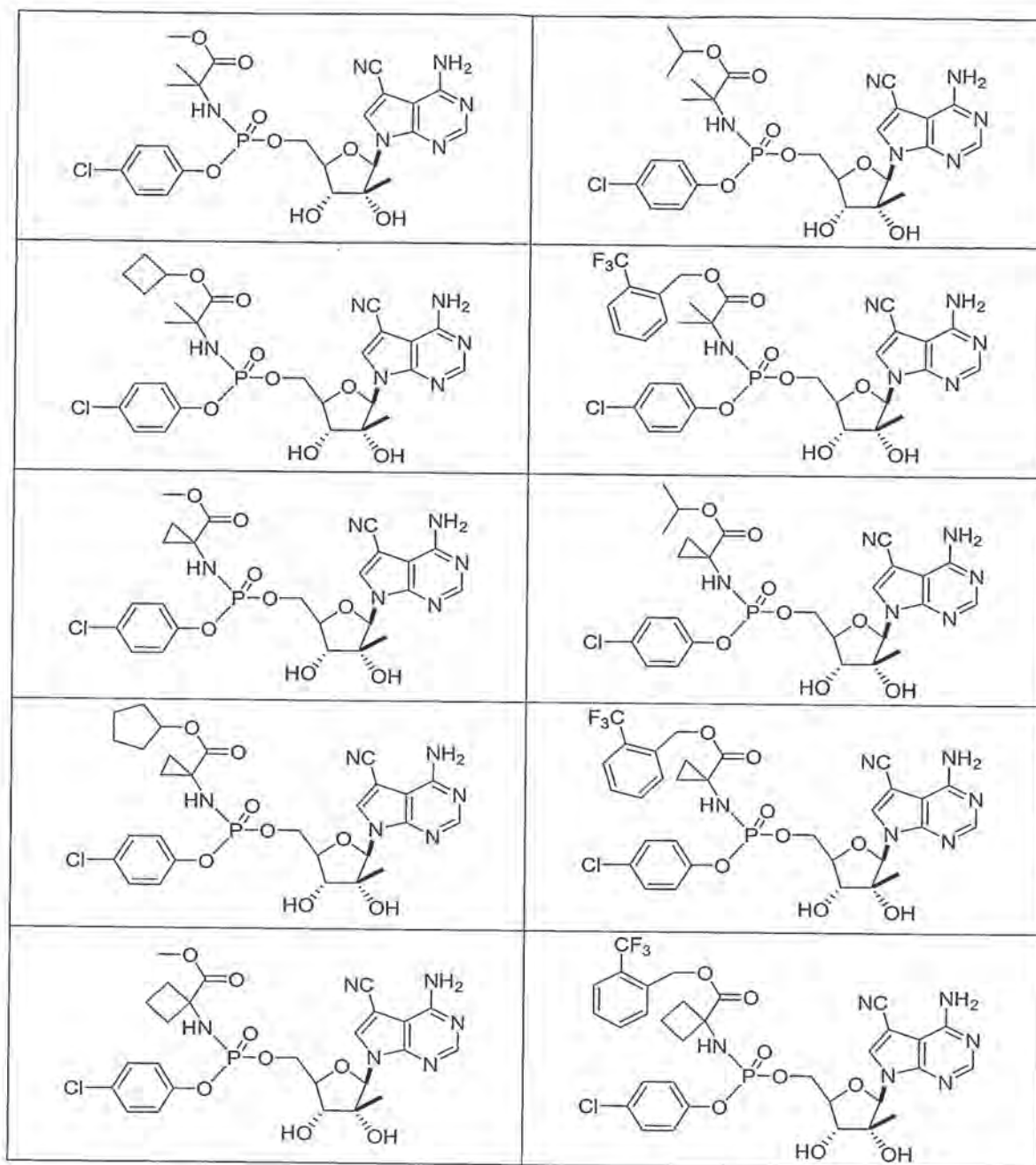


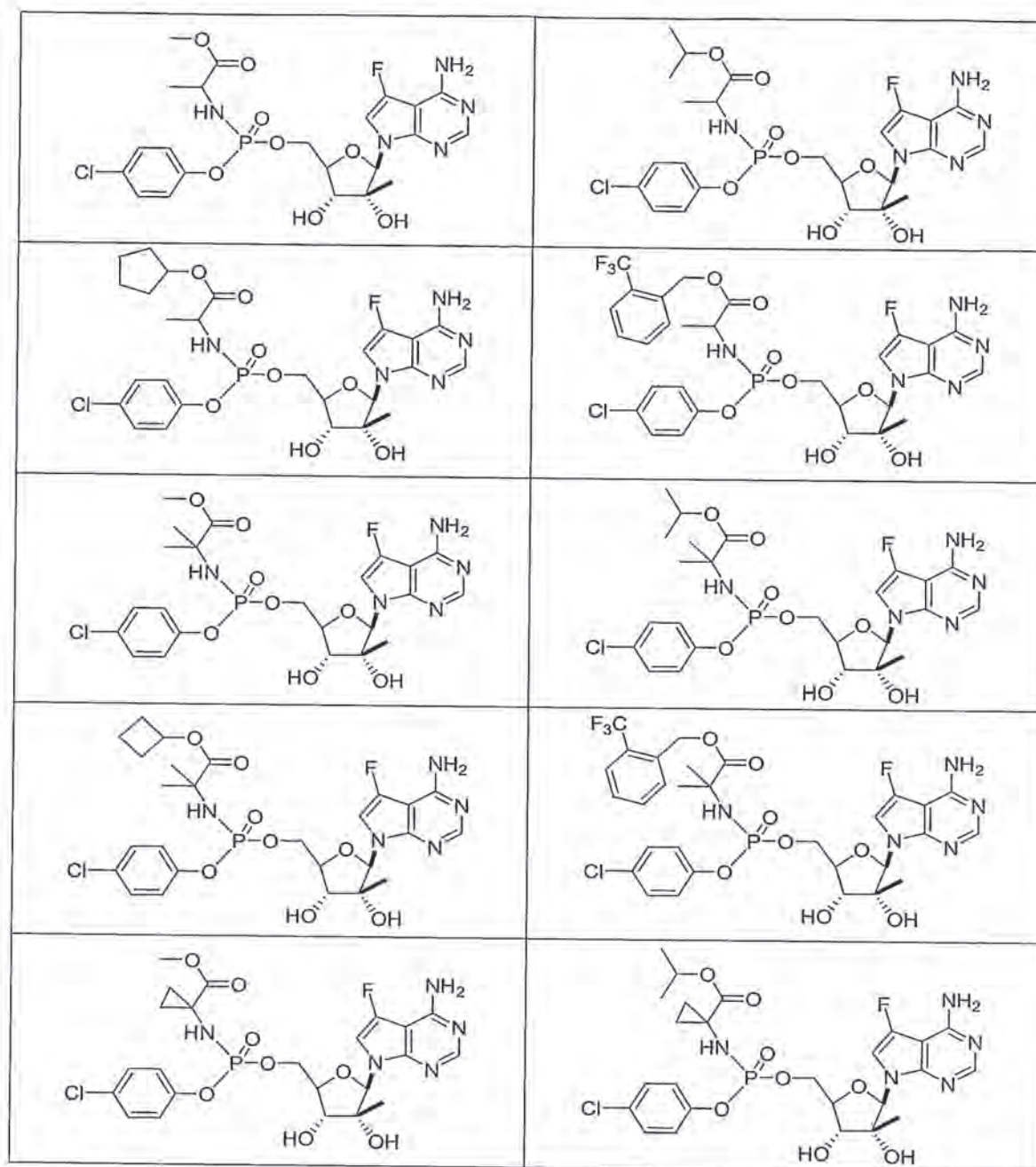


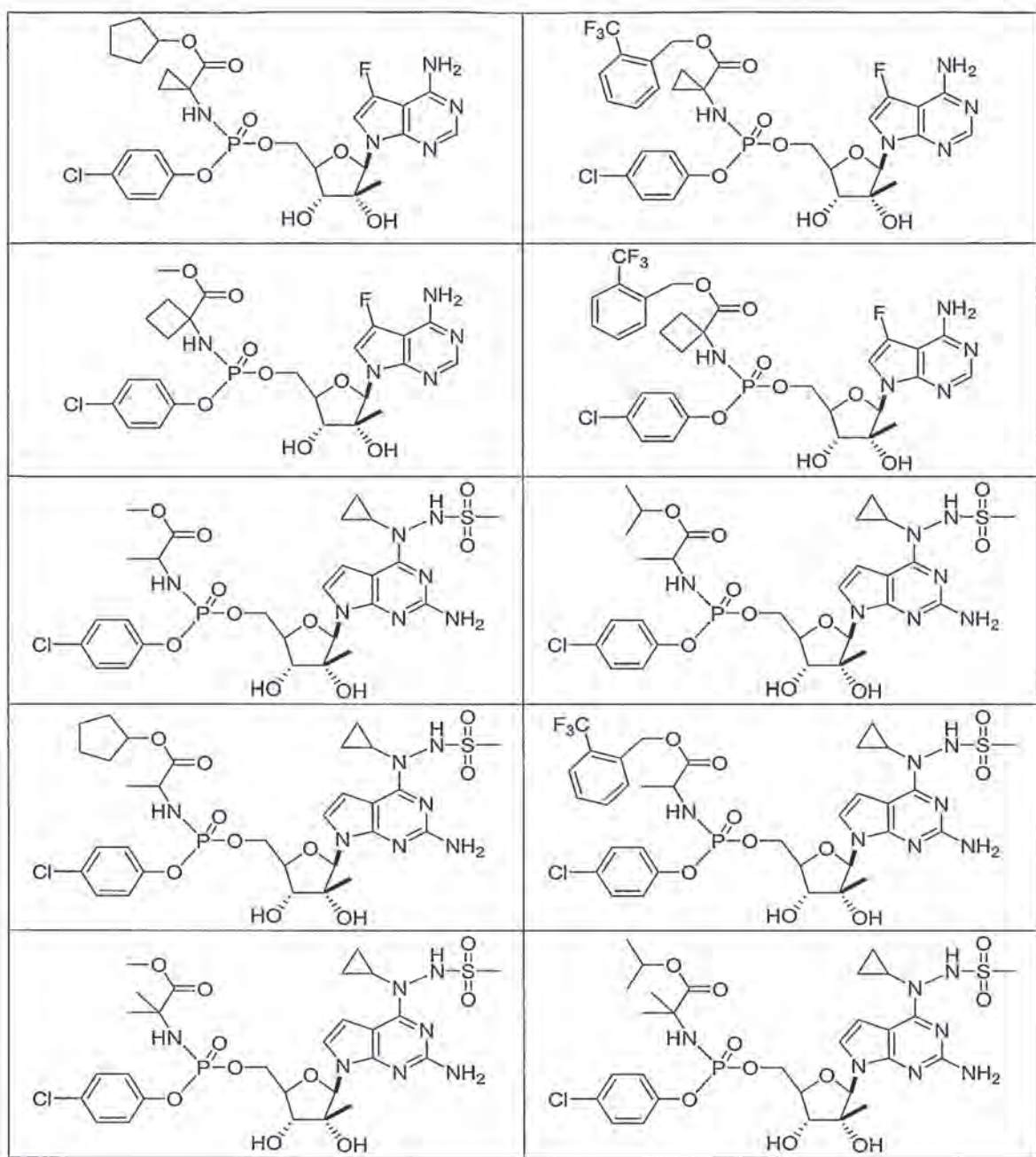


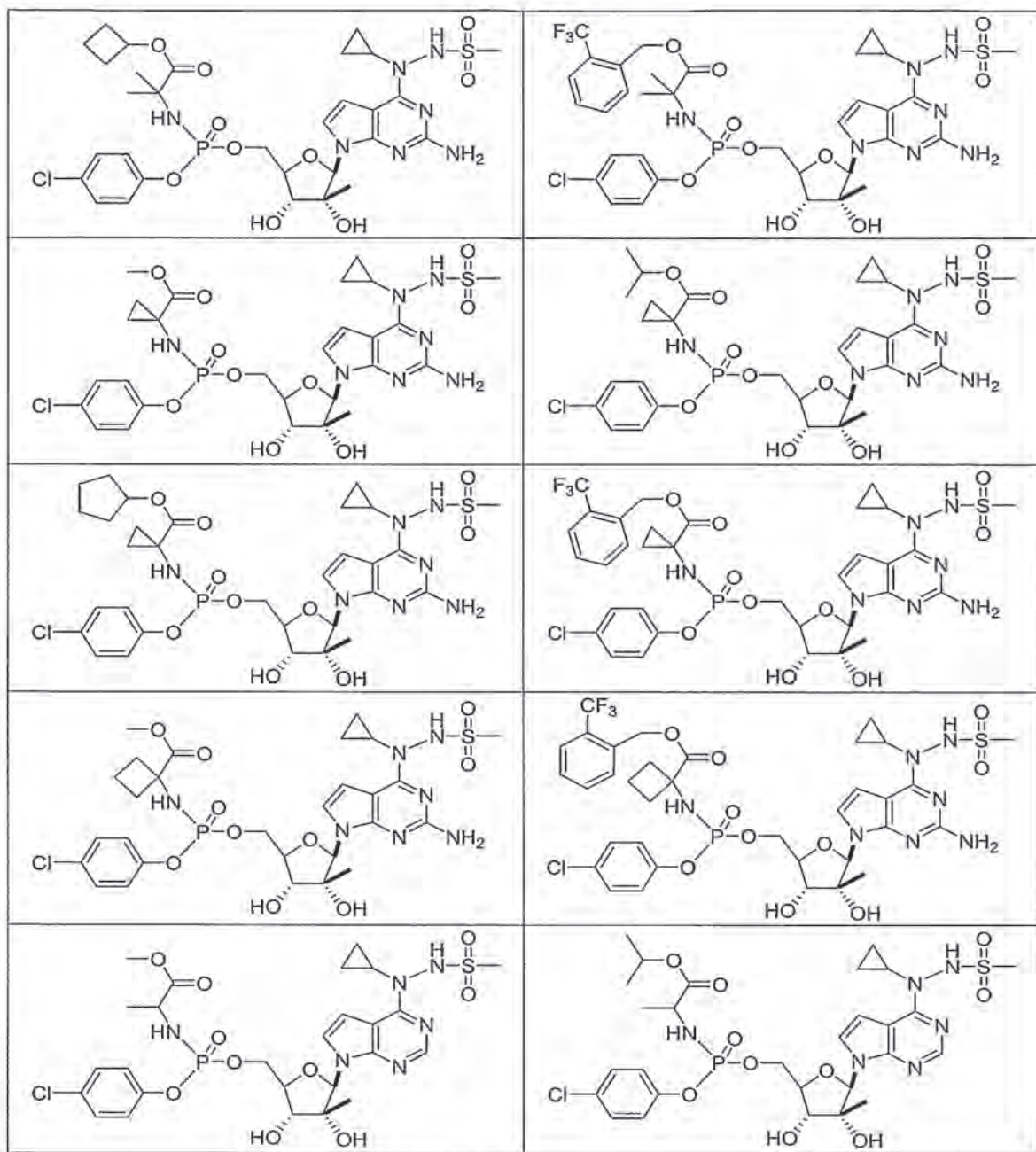


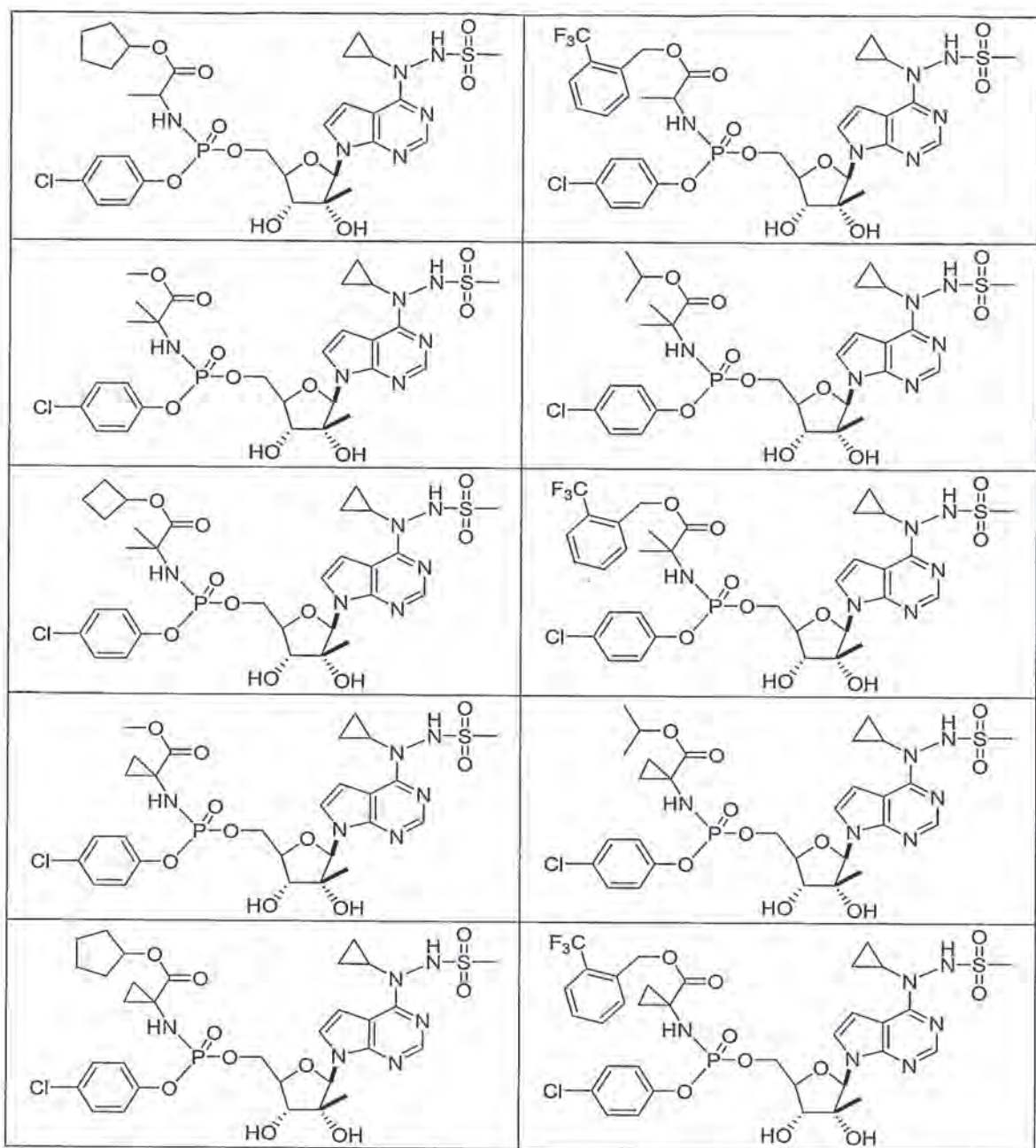


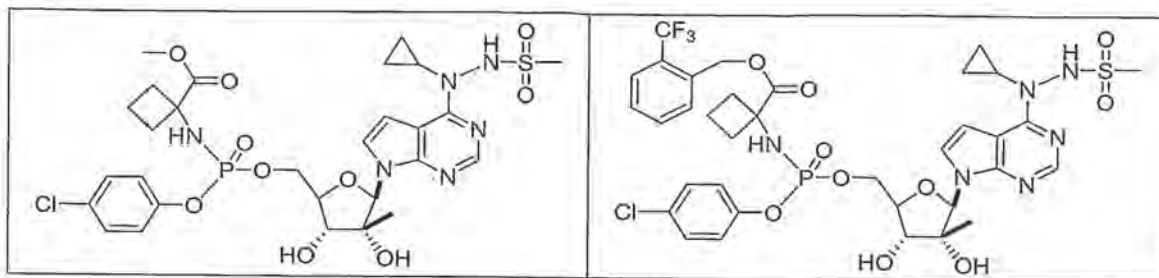








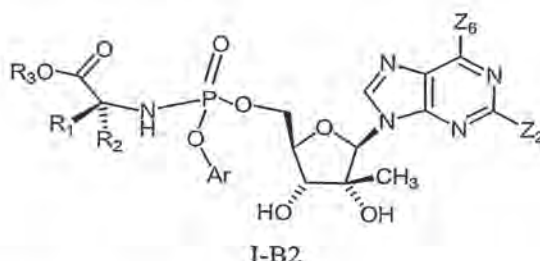




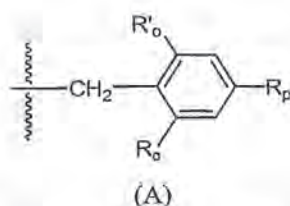
Claims

What is claimed is

- 5 1. A compound of formula I-B2



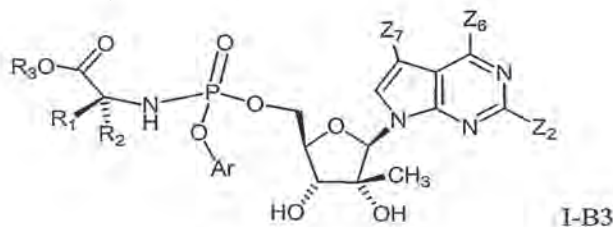
- 10 where Ar is phenyl, pyridyl, or pyrimidyl, optionally substituted with one or two groups selected independently from halo, nitro, cyano, C₁-C₃ alkyl, or C₁-C₃ alkoxy, wherein said C₁-C₃ alkyl group, and the C₁-C₃ alkyl moiety of said C₁-C₃ alkoxy group are optionally substituted with one, two, or three chlorine or fluorine atoms;
- R_1 and R_2 are, independently, H, C₁-C₅ alkyl, or C₂-C₅ alkenyl, or R_1 and R_2 , together with the
- 15 α -carbon, form a 3- to 6- membered saturated ring;
- R_3 is C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkyl methyl, benzyl, or phenethyl, in which the phenyl group within said benzyl or phenethyl group is optionally substituted with one or more groups selected independently from halogen, C₁-C₆ alkyl, and C₁-C₆ alkoxy, wherein said C₁-C₃ alkyl group, and the C₁-C₃ alkyl moiety of said C₁-C₃ alkoxy group are optionally
- 20 substituted with one, two, or three chlorine or fluorine atoms;
- Z^2 = H, NH₂, NHMe, or NMe₂; and
- Z^6 = OH or NR₄R₅, where R_4 is H, C₁-C₄ alkyl, or cyclopropyl; R_5 is H or NHR₆; R_6 is H, C₁-C₄ alkyl, or SO₂R₇; and R_7 is C₁-C₄ alkyl, and wherein all tautomeric forms are included.
- 25 2. The compound of claim 1, where Ar is phenyl, optionally substituted as described in claim 1.
3. The compound of claim 2, where Ar is unsubstituted phenyl, p-chlorophenyl, or p-bromophenyl.
- 30 4. The compound of claim 3, where R_3 is benzyl or phenethyl, optionally substituted as indicated in claim 1.
5. The compound of claim 4, where R_3 is a group of formula A



where R_p , R_o , and R'_o are selected independently from H, methyl, F, Cl, methoxy, and trifluoromethyl.

- 5
6. The compound of claim 5, where R_p is H, except when R_o and R'_o are both methyl; and when R_o and R'_o are both methyl, R_p is methyl, halogen, or trifluoromethyl.
7. The compound of claim 6, where R_o is H.
- 10 8. The compound of claim 7, where R'_o is H.
9. The compound of claim 2, where R_3 is C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, or C_3 - C_6 cycloalkyl methyl.
10. The compound of claim 9, where R_3 is C_1 - C_4 alkyl.
11. The compound of claim 9, where R_3 is C_3 - C_6 cycloalkyl
- 15 12. The compound of claim 3 or claim 9, where Z^2 is H or NH_2 and Z^6 is NR_4R_5 .
13. The compound of claim 12, where R_5 is H or NHR_6 ; R_6 is H, methyl, or SO_2R_7 ; and R_7 is CH_3 .
14. The compound of claim 12, where R_4 cyclopropyl or methyl.
15. A compound of Formula 1-B3

20



- where Ar is phenyl, pyridyl, or pyrimidyl, optionally substituted with one or two groups
- 25 selected independently from halo, nitro, cyano, C_1 - C_3 alkyl, or C_1 - C_3 alkoxy, wherein said C_1 -

C₃ alkyl group, and the C₁-C₃ alkyl moiety of said C₁-C₃ alkoxy group are optionally substituted with one, two, or three chlorine or fluorine atoms;

R₁ and R₂ are, independently, H, C₁-C₅ alkyl, or C₂-C₅ alkenyl, or R₁ and R₂, together with the α -carbon, form a 3- to 6- membered saturated ring;

- 5 R₃ is C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkyl methyl, benzyl, or phenethyl, in which the phenyl group within said benzyl or phenethyl group is optionally substituted with one or more groups selected independently from halogen, C₁-C₆ alkyl, and C₁-C₆ alkoxy, wherein said C₁-C₃ alkyl group, and the C₁-C₃ alkyl moiety of said C₁-C₃ alkoxy group are optionally substituted with one, two, or three chlorine or fluorine atoms;
- 10 Z² = H, NH₂, NHMe, or NMe₂;
 Z⁶ = OH or NR₄R₅, where R₄ is H, C₁-C₄ alkyl, or cyclopropyl; R₅ is H or NHR₆; R₆ is H, C₁-C₄ alkyl, or SO₂R₇; R₇ is C₁-C₄ alkyl; Z⁷ is H, halogen, or CN; and wherein all tautomeric forms are included.

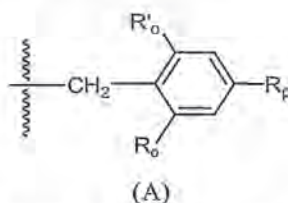
16. The compound of claim 15 where Ar is phenyl, optionally substituted as described in

- 15 claim 15.

17. The compound of claim 16, where Ar is unsubstituted phenyl, *p*-chlorophenyl, or *p*-bromophenyl.

18. The compound of claim 17, where R₃ is benzyl or phenethyl, optionally substituted as described in claim 15.

- 20 19. The compound of claim 18, where R₃ is a group of formula A



where R_p, R₀, and R'₀ are selected independently from H, methyl, F, Cl, methoxy, and

- 25 trifluoromethyl.

20. The compound of claim 19, where R_p is H, except when R_o and R'_o are both methyl; and when R_o and R'_o are both methyl, R_p is methyl, halogen, or trifluoromethyl.

21. The compound of claim 20, where R_o is H.

5 22. The compound of claim 21, where R_o' is H.

23. The compound of claim 16, where R_3 is C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, or C_3 - C_6 cycloalkyl methyl.

24. The compound of claim 23, where R_3 is C_1 - C_4 alkyl.

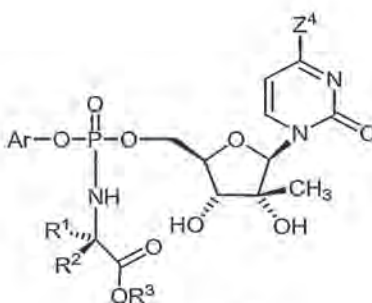
25. The compound of claim 23, where R_3 is C_3 - C_6 cycloalkyl.

10 26. The compound of claim 17 or claim 23, Z^2 is H or NH_2 and Z^6 is NR_4R_5 .

27. The compound of claim 26, where R_5 is H or NHR_6 ; R_6 is H, methyl, or SO_2R_7 ; and R_7 is CH_3 .

28. The compound of claim 27, where Z_7 is H or F.

29. A compound of formula I-B1



IB-1

15 where Z^4 is OH or NH_2 and where Ar is phenyl, pyridyl, or pyrimidyl, optionally substituted with one or two groups selected independently from halo, nitro, cyano, C_1 - C_3 alkyl, or C_1 - C_3 alkoxy, wherein said C_1 - C_3 alkyl group, and the C_1 - C_3 alkyl moiety of said C_1 - C_3 alkoxy group are optionally substituted with one, two, or three chlorine or fluorine atoms;

20 R_1 and R_2 are, independently, H, C_1 - C_5 alkyl, or C_2 - C_5 alkenyl, or R_1 and R_2 , together with the α -carbon, form a 3- to 6- membered saturated ring;

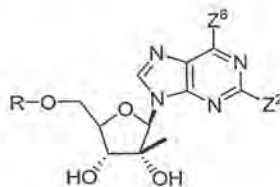
R_3 is C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, C_3 - C_6 cycloalkyl methyl, benzyl, or phenethyl, in which the phenyl group within said benzyl or phenethyl group is optionally substituted with one or

25 more groups selected independently from halogen, C_1 - C_6 alkyl, and C_1 - C_6 alkoxy, wherein said

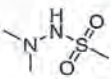
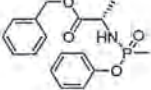
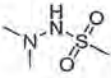
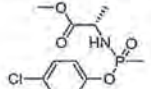
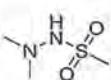
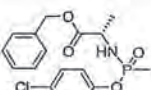
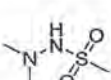
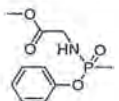
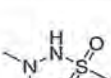
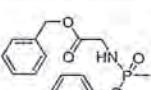
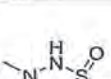
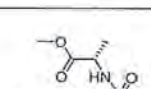
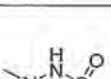
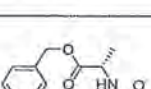
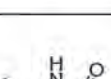
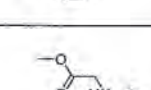
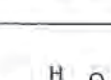
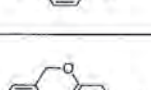
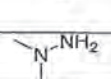
C₁-C₃ alkyl group, and the C₁-C₃ alkyl moiety of said C₁-C₃ alkoxy group are optionally substituted with one, two, or three chlorine or fluorine atoms.

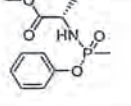
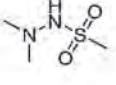
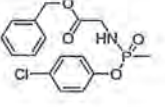
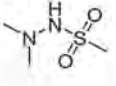
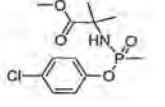
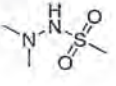
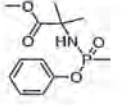
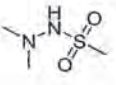
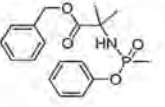
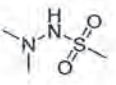
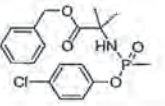
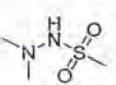
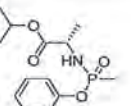
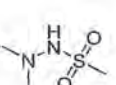
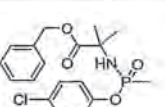
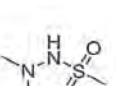
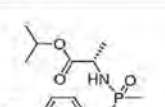
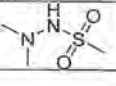
30. The compound of claim 29, where Ar is phenyl, optionally substituted as described al

5 31. A compound of formula I-B2 which is selected from the following table

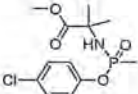
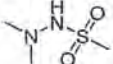
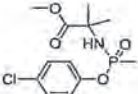
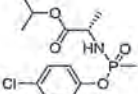
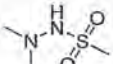
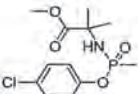
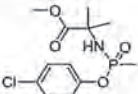
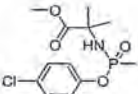
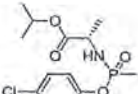
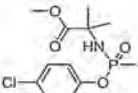


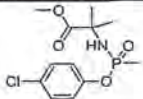
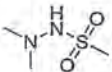
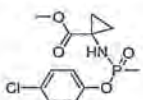
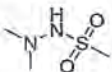
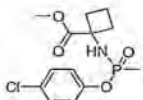
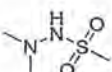
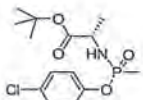
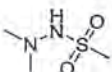
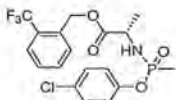
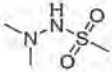
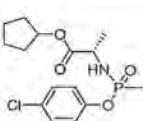
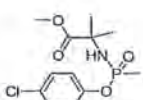
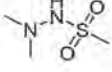
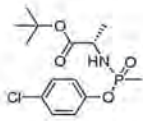
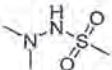
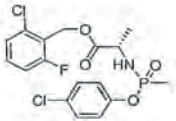
Z ²	Z ⁶	R
H		
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NH ₂		
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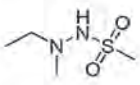
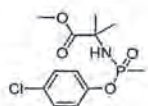
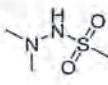
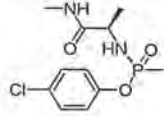
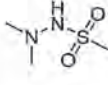
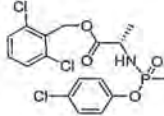
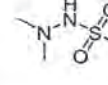
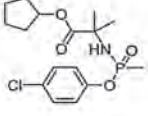
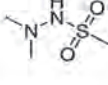
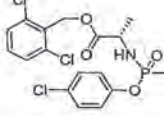
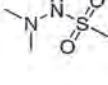
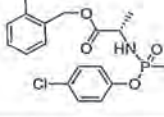
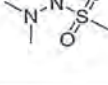
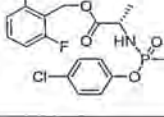
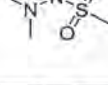
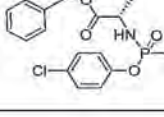
Z^2	Z^3	R
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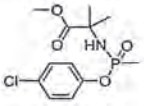
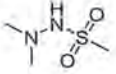
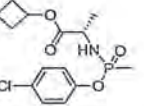
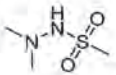
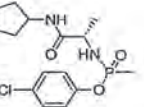
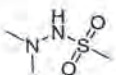
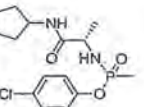
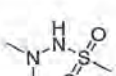
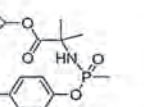
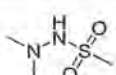
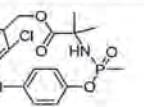
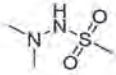
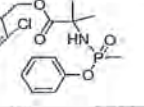
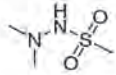
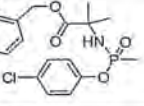
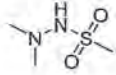
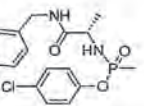
Z ²	Z ⁶	R
		
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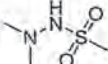
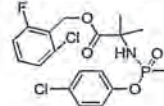
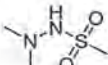
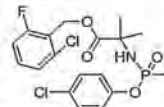
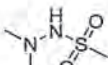
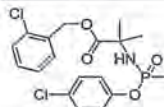
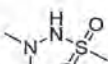
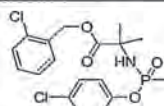
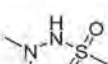
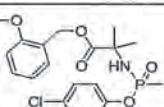
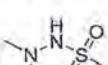
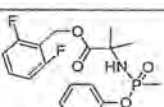
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H	NHMe	
NH ₂		
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NH ₂	NH ₂	

Z ²	Z ⁶	R
		
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Z ²	Z ⁶	R
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NH ₂		
H		

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US06/17314

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C07H 19/04(2006.01)
A01N 43/04(2006.01);A61K 31/70(2006.01)

USPC: 536/26.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/26.1, 27.1, 27.13, 28.1; 514/43

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAPLUS, WEST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KUMPULAINEN et al. "An Efficient Strategy for the Synthesis of 1-Chloroethyl Phosphates and Phosphoramidates", J. Org. Chem., 2005, Vol. 70, pages 9056-9058.	1-31
A	US 6,245,750 (SHEPARD) 12 June 2001 (12.06.2001).	1-31

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search
19 August 2006 (19.08.2006)

Date of mailing of the international search report

20 SEP 2006

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Authorized officer

Patrick A. Lewis

Telephone No. 571-272-1600

Form PCT/ISA/210 (second sheet) (April 2005)

Electronic Acknowledgement Receipt	
EFS ID:	11522405
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	23552
Filer:	Daniel R. Evans
Filer Authorized By:	
Attorney Docket Number:	60137.0034USC1
Receipt Date:	01-DEC-2011
Filing Date:	03-MAY-2011
Time Stamp:	15:01:37
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		13099671_IDS_PTO1449_1_61 037_0034USC1.pdf	105216 2f0306e0ac27c0b4989c010cc0d1170259c810	yes	3

	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
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	Information Disclosure Statement (IDS) Form (SB08)		2	3	
Warnings:					
Information:					
2	Foreign Reference	WO06121820.pdf	4158785	no	147
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3	Non Patent Literature	Aquaro.pdf	75674	no	5
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Total Files Size (in bytes):			9491003		

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Sofia et al.	Examiner:	Lewis
Application No.:	13/099,671	Group Art Unit:	1623
Filed:	May 3, 2011	Docket No.:	60137.0034USC1
Title:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS		

INFORMATION DISCLOSURE STATEMENT (37 C.F.R. § 1.97(b))

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

Dear Sir:

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner.

No fee is due for consideration of the items listed on the enclosed Form 1449.

No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the reference(s) are not "prior art."³³ Moreover, Applicants do not represent that a reference has been thoroughly reviewed or that any relevance of any portion of a reference is intended.

Consideration of the items listed is respectfully requested. Pursuant to the provisions of M.P.E.P. 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

Please charge any additional fees or credit any overpayment to Deposit Account No. 13-2725.



Respectfully submitted,
MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300
/Daniel R. Evans/
Daniel R. Evans, Ph.D.
Reg. No. 55,868

FORM 1449* INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary)	Docket Number: 60137.0034USC1	Application Number: 13/099,671
	Applicant: Sofia et al	
	Filing Date: May 3, 2011	Group Art Unit: 1623

OTHER DOCUMENTS		
		U.S. Patent No. 7,964,580, which issued from US 12/053,015 – Cover Page and Issued Claims.
		Selected Prosecution Documents from US 12/053,015: (1) June 15, 2010 Restriction Requirement; (2) October 28, 2010 Amendment; (3) January 5, 2011 Notice of Allowance; and (4) April 1, 2011 Amendment.
		US 12/783,680, filed May 20, 2010 – Originally filed claims.
		US 13/076,552, filed March 31, 2011 – Originally filed claims.
		US 12/645,710, filed December 23, 2009 – Originally filed claims.
		U.S. Patent No. 7,429,572, which issued from US 10/828,753 – Cover Page and Issued Claims.
		Selected Prosecution Documents from US 10/828,753: (1) February 26, 2007 Amendment; (2) March 30, 2007 Office Action; (3) June 19, 2007 Interview Summary; (4) September 12, 2007 Amendment; (5) September 12, 2007 Declaration; (6) September 24, 2007 Declaration; (7) November 28, 2007 Amendment; (8) February 26, 2008 Office Action; (9) March 11, 2008 Amendment; and (10) May 29, 2008 Notice of Allowance
		US 11/854,218 – Pending Claims as of June 28, 2011
		Selected Prosecution Documents for US 11/854,218: (1) September 12, 2007 Amendment; (2) October 1, 2009 Office Action; (3) March 31, 2010 Response; (4) March 31, 2011 Declaration; (5) July 22, 2010 Office Action; (6) October 11, 2010 Amendment; (7) October 11, 2010 Declaration; (8) December 23, 2010 Office Action; (9) June 28, 2011 Amendment.
		US 12/878,262 – Pending Claims as of September 1, 2011
		Selected Prosecution Documents for US 12/878,262: (1) September 9, 2010 Amendment; (2) June 8, 2011 Office Action; and (3) September 1, 2011 Amendment.

23552 PATENT TRADEMARK OFFICE	EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

Electronic Acknowledgement Receipt	
EFS ID:	11529768
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	23552
Filer:	Daniel R. Evans/AMY ALBA
Filer Authorized By:	Daniel R. Evans
Attorney Docket Number:	60137.0034USC1
Receipt Date:	02-DEC-2011
Filing Date:	03-MAY-2011
Time Stamp:	12:14:11
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		13099671_IDS_PTO1449_2_60 137_0034USC1.pdf	224957 5a2c37c01ab1e60449c44946b09e671ae26c + 0822	yes	8

Multipart Description/PDF files in .zip description					
Document Description			Start	End	
Transmittal Letter			1	7	
Information Disclosure Statement (IDS) Form (SB08)			8	8	
Warnings:					
Information:					
2	Non Patent Literature	13099671_Dec2_2011_IDS_OtherDocuments_60137_0034usc1.pdf	13112126	no	359
Warnings:					
Information:					
Total Files Size (in bytes):			13337083		
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.					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Sofia et al.	Examiner:	Lewis
Application No.:	13/099,671	Group Art Unit:	1623
Filed:	May 3, 2011	Docket No.:	60137.0034USC1
Title:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS		

INFORMATION DISCLOSURE STATEMENT (37 C.F.R. § 1.97(b))

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

Dear Sir:

This statement should be considered because it is submitted before the mailing date of a first Office Action. Accordingly, no fee is due for consideration of the items listed on the enclosed Form 1449.

Applicants request that the Examiner consider the pending claims of the present application in view of the pending or issued claims of the following patents and patent applications:

- (1) U.S. Patent No. 7,964,580 ("the '580 patent");
- (2) U.S. Patent Application No. 12/783,680 ("the '680 application");
- (3) U.S. Patent Application No. 13/076,552 ("the '552 application");
- (4) U.S. Patent Application No. 12/645,710 ("the '710 application");
- (5) U.S. Patent No. 7,429,572 ("the '572 patent");
- (6) U.S. Application No. 11/854,218 ("the '218 application"); and
- (7) U.S. Application No. 12/878,262 ("the '262 application").

Certain aspects of the claimed subject matter in these issued patents and pending applications are summarized below. Applicants have cited and attached herewith the issued claims of the patents and the presently pending claims of the applications. Applicants have also cited and attached herewith selected prosecution documents of the patents and pending application. Applicants respectfully request that the Examiner acknowledge consideration of this information and provide an indication of the same by returning the initialed, signed, and dated modified PTO-1449 form with the first Office Action.

- (1) The '580 patent issued on June 21, 2011, from US 12/053,015. The present application is a continuation of the '580 patent.

Claims 1 and 8 of the '580 patent recite:

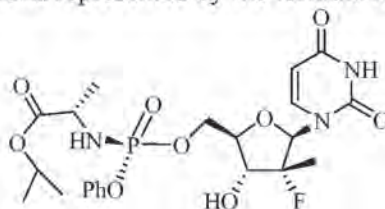
1. (S)-2-{{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester or a stereoisomer thereof.

8. (S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

- (2) The '680 application, was filed on May 20, 2010 and claims priority to US 61/179,923, filed on May 20, 2009 and US 61/319,513, filed March 31, 2010.

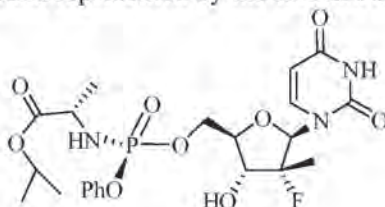
Claims 13 and 35 of the '680 application recite:

13. A compound represented by the formula R_p-4



R_p-4

35. A compound represented by the formula S_p-4



S_p-4

- (3) The '552 application was filed on March 31, 2011. The '552 application is a continuation-in-part of the '680 application. In addition to the '680 application, the '552 application claims priority to US 61/319,513, filed on March 31, 2010 and US 61/319,548, filed March 31, 2010.

Claims 1-2 of the '552 application recite:

1. Crystalline (S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

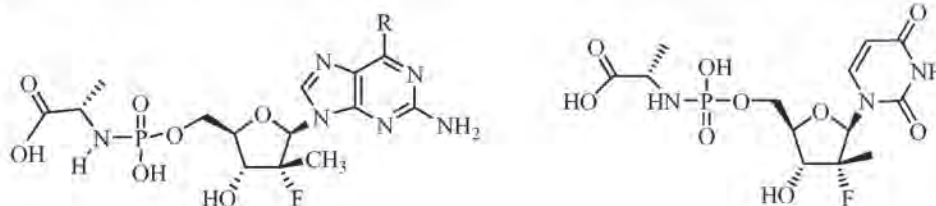
2. Crystalline (S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate having:

- (1) XRPD 2 θ -reflections ($^{\circ}$) at about: 5.2, 7.5, 9.6, 16.7, 18.3, and 22.2;
- (2) XRPD 2 θ -reflections ($^{\circ}$) at about: 5.0, 7.3, 9.4, and 18.1;
- (3) XRPD 2 θ -reflections ($^{\circ}$) at about: 4.9, 6.9, 9.8, 19.8, 20.6, 24.7, and 26.1;
- (4) XRPD 2 θ -reflections ($^{\circ}$) at about: 6.9, 9.8, 19.7, 20.6, and 24.6;
- (5) XRPD 2 θ -reflections ($^{\circ}$) at about: 5.0, 6.8, 19.9, 20.6, 20.9, and 24.9;
- (6) XRPD 2 θ -reflections ($^{\circ}$) at about: 5.2, 6.6, 7.1, 15.7, 19.1, and 25.0; or
- (7) XRPD 2 θ -reflections ($^{\circ}$) at about: 6.1, 8.2, 10.4, 12.7, 17.2, 17.7, 18.0, 18.8, 19.4, 19.8, 20.1, 20.8, 21.8, and 23.3.;

- (4) U.S. Patent Application No. 12/645,710 ("the '710 application") filed December 23, 2009, which claims priority to US 61/140,441, filed on December 23, 2008.

Claim 1 of the '710 application recites:

1. A purified compound represented by formula **I** or a purified compound represented by formula **II**, a salt, a pharmaceutically acceptable salt, a hydrate, a solvate, or a crystalline form thereof:



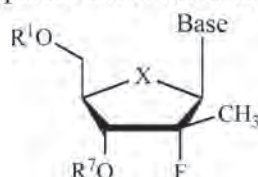
I

II

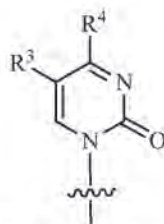
wherein R is OMe, OEt, -N(-CH₂CH₂CH₂-) (azetidin-1-yl), or OH;
 or a salt, a pharmaceutically acceptable salt, a hydrate, a solvate, or a crystalline form thereof.

- (5) U.S. Patent No. 7,429,572 ("the '572 patent") issued on September 30, 2008, which issued from U.S. Application No. 10/828,753, filed April 21, 2004 and published as US 2005/0009737 on January 13, 2005.

Claim 1 of the '572 patent is directed to a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β -D or β -L) or its pharmaceutically acceptable salt of the structure:



wherein the Base is a pyrimidine base represented by the following formula



X is O; R¹ and R⁷ are independently H, a monophosphate, a diphosphate, a triphosphate, a H-phosphonate, an alkyl, an alkyl sulfonyl, or an arylalkyl sulfonyl; and R³ is H and R⁴ is NH₂ or OH.

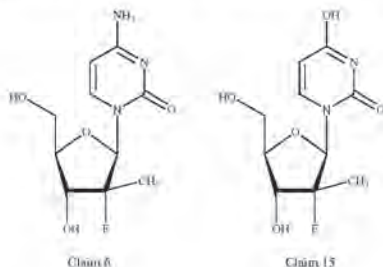
Claims 2-4 of the '572 patent recite:

2. The (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β-D or β-L) of claim 1 or its pharmaceutically acceptable salt thereof, wherein R⁷ is H and R¹ is a monophosphate, or diphosphate, or a triphosphate.

3. The (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β-D) of claim 1 or its pharmaceutically acceptable salt thereof, R⁷ is H and R¹ is a diphosphate or a triphosphate.

4. A (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β-D or β-L) of claim 1 or its pharmaceutically acceptable salt thereof wherein R⁷ is H and R¹ is a triphosphate.

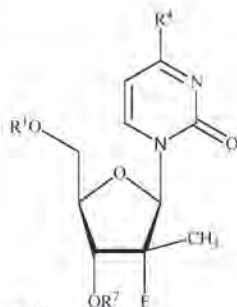
Claims 6 and 15 of the '572 patent are directed to the respective compounds or its pharmaceutically acceptable salt:



(6) U.S. Application No. 11/854,218 ("the '218 application") claims priority to the '572 patent. As noted above, a copy of the pending claims are attached herewith.

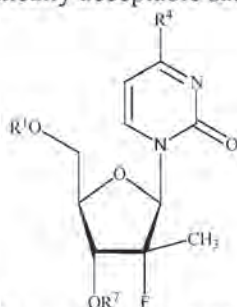
Claims 149-152 of the '218 application recite:

149. A method for the treatment of hepatitis C infection, which comprises administering to a mammal in need thereof an anti-virally effective amount of a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β-D) or its pharmaceutically acceptable salt of the structure:



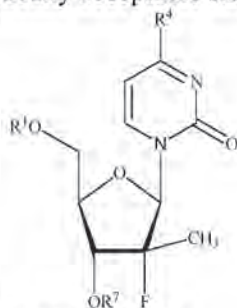
wherein R^1 and R^7 are both H; and R^4 is OH.

150. A method for the treatment of hepatitis C infection, which comprises administering to a mammal in need thereof an anti-virally effective amount of a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β -D) or its pharmaceutically acceptable salt of the structure:



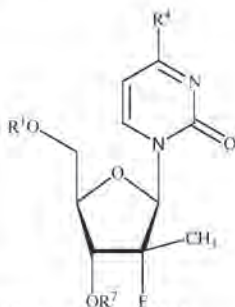
wherein R^1 monophosphate and R^7 is H; and R^4 is OH.

151. A method for the treatment of hepatitis C infection, which comprises administering to a mammal in need thereof an anti-virally effective amount of a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β -D) or its pharmaceutically acceptable salt of the structure:



wherein R^1 diphosphate and R^7 is H; and R^4 is OH.

152. A method for the treatment of hepatitis C infection, which comprises administering to a mammal in need thereof an anti-virally effective amount of a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β -D) or its pharmaceutically acceptable salt of the structure:

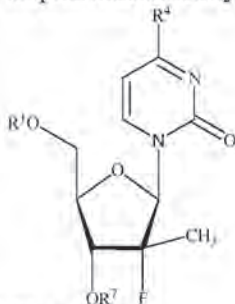


wherein R^1 triphosphate and R^7 is H; and R^4 is OH.

(7) U.S. Application No. 12/878,262 ("the '262 application") claims priority to the '572 patent. As noted above, a copy of the pending claims are attached herewith.

Claims 149-152 of the '218 application recite:

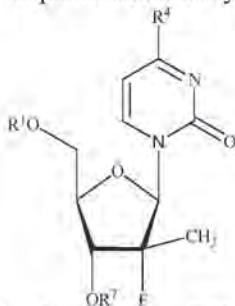
174. A method of inhibiting the proliferation of a Flaviviridae virus in a host comprising penetrating a cell infected with the virus with an antivirally effective amount of a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β -D) or its pharmaceutically acceptable salt of the structure:



wherein R^1 and R^7 are both H; and R^4 is OH.

175. The method of claim 174, wherein the Flaviviridae virus is hepatitis C virus.

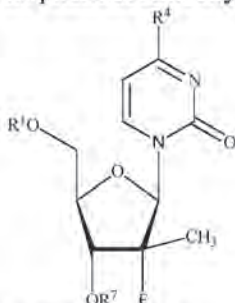
177. A method of inhibiting the proliferation of a Flaviviridae virus in a host comprising penetrating a cell infected with the virus with an antivirally effective amount of a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β -D) or its pharmaceutically acceptable salt of the structure:



wherein R^1 monophosphate and R^7 is H; and R^4 is OH.

178. The method of claim 177, wherein the Flaviviridae virus is hepatitis C virus.

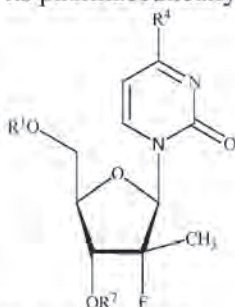
179. A method of inhibiting the proliferation of a Flaviviridae virus in a host comprising penetrating a cell infected with the virus with an antivirally effective amount of a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β -D) or its pharmaceutically acceptable salt of the structure:



wherein R^1 diphosphate and R^7 is H; and R^4 is OH.

180. The method of claim 179, wherein the Flaviviridae virus is hepatitis C virus.

181. A method of inhibiting the proliferation of a Flaviviridae virus in a host comprising penetrating a cell infected with the virus with an antivirally effective amount of a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β -D) or its pharmaceutically acceptable salt of the structure:



wherein R^1 triphosphate and R^7 is H; and R^4 is OH.

182. The method of claim 181, wherein the Flaviviridae virus is hepatitis C virus.

Consideration of the items listed is respectfully requested. Pursuant to the provisions of M.P.E.P. 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

Please charge any required fees or credit any overpayment to Deposit Account No. 13-2725.



Date: December 2, 2011

Respectfully submitted,
MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300
/Daniel R. Evans/

Daniel R. Evans. Ph.D.
Reg. No. 55,868



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.
13/099,671	05/03/2011	Michael Joseph Sofia	60137.0034USC1	1344

23552 7596 12/05/2011
MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER

LEWIS, PATRICK T

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

1623

MAIL DATE	DELIVERY MODE
-----------	---------------

12/05/2011

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	13/099,671	SOFIA ET AL.	
	Examiner	Art Unit	
	PATRICK LEWIS	1623	

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

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ 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.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 2 and 13-30 is/are pending in the application.
- 5a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 6) ☒ Claim(s) 15-23 is/are allowed.
- 7) ☒ Claim(s) 2, 13, 14 and 24-30 is/are rejected.
- 8) ☐ Claim(s) _____ is/are objected to.
- 9) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some c) ☐ None of:
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)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) ☐ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413) |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) ☒ Information Disclosure Statement(s) (PTO/SB/08) | 5) ☐ Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12022011; 12012011</u> | 6) ☐ Other: _____ |

DETAILED ACTION

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 2, 13-14 and 24-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 7,964,580. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The examined claims are either anticipated by, or would have been obvious over, the reference claim(s). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are generic to all that is recited in claims 1-14 of U.S. Patent No. 7,964,580. That is, claims 1-14 of U.S. Patent No. 7,964,580 fall entirely within the scope of claims 2, 13-14 and 24-30 or, in other words, claims 2, 13-14 and 24-30 are anticipated by claims 1-14 of U.S. Patent No. 7,964,580.

Conclusion

3. Claims 2 and 13-30 are pending. Claims 2, 13-14 and 24-30 are rejected. Claims 15-23 are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PATRICK LEWIS whose telephone number is (571)272-

Application/Control Number: 13/099,671
Art Unit: 1623

Page 4

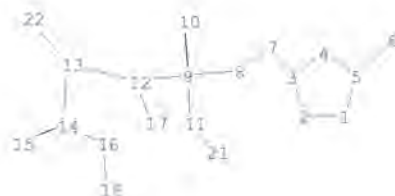
0655. The examiner can normally be reached on Monday - Thursday 10 am to 3 pm (Maxi Flex).

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

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

/Patrick T. Lewis/
Primary Examiner, Art Unit 1623

/PL/



chain nodes :

6 7 8 9 10 11 12 13 14 15 16 17 18 21 22

ring nodes :

1 2 3 4 5

chain bonds :

3-7 5-6 7-8 8-9 9-10 9-11 9-12 11-21 12-13 12-17 13-14 13-22 14-15 14-16 16-18

ring bonds :

1-2 1-5 2-3 3-4 4-5

exact/norm bonds :

1-2 1-5 2-3 3-4 4-5 5-6 7-8 8-9 9-10 9-11 9-12 11-21 12-13 14-15 14-16 16-18

exact bonds :

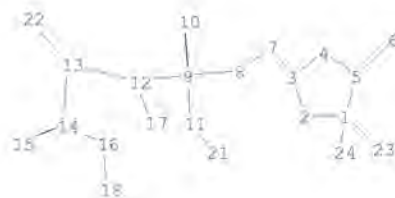
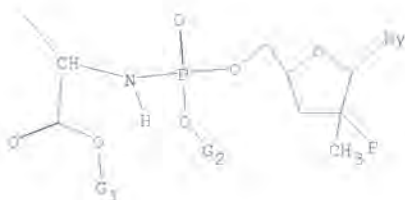
3-7 12-17 13-14 13-22

G1:CH3,CH2,Et,n-Pr,i-Pr,n-Bu,i-Bu,t-Bu

G2:H,p-C6H4

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 21:CLASS 22:CLASS



```

chain nodes :
  6  7  8  9  10 11 12 13 14 15 16 17 18 21 22 23 24
ring nodes :
  1  2  3  4  5
chain bonds :
  1-23 1-24 3-7 5-6 7-8 8-9 9-10 9-11 9-12 11-21 12-13 12-17 13-14 13-22 14-15
  14-16 16-18
ring bonds :
  1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
  1-2 1-5 2-3 3-4 4-5 5-6 7-8 8-9 9-10 9-11 9-12 11-21 12-13 14-15 14-16 16-18
exact bonds :
  1-23 1-24 3-7 12-17 13-14 13-22
  
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G1:CH3,CH2,Et,n-Pr,i-Pr,n-Bu,i-Bu,t-Bu

G2:H,p-C6H4

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Match level :
  1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS
  12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 21:CLASS 22:CLASS
  23:CLASS 24:CLASS
  
```

<i>Index of Claims</i> 	Application/Control No. 13099671	Applicant(s)/Patent Under Reexamination SOFIA ET AL.
	Examiner PATRICK LEWIS	Art Unit 1623

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

☐ Claims renumbered in the same order as presented by applicant		☐ CPA		☐ T.D.		☐ R.1.47	
CLAIM		DATE					
Final	Original	12/04/2011					
	1	-					
	2	✓					
	3	-					
	4	-					
	5	-					
	6	-					
	7	-					
	8	-					
	9	-					
	10	-					
	11	-					
	12	-					
	13	✓					
	14	✓					
	15	=					
	16	=					
	17	=					
	18	=					
	19	=					
	20	=					
	21	=					
	22	=					
	23	=					
	24	✓					
	25	✓					
	26	✓					
	27	✓					
	28	✓					
	29	✓					
	30	✓					

(FILE 'HOME' ENTERED AT 21:29:15 ON 04 DEC 2011)

FILE 'REGISTRY' ENTERED AT 21:29:23 ON 04 DEC 2011

L1 STRUCTURE UPLOADED

L2 50 S L1 SSS SAM

L3 1300 S L1 SSS FULL

FILE 'CAPLUS, MEDLINE' ENTERED AT 21:30:04 ON 04 DEC 2011

L4 315 S L3

FILE 'REGISTRY' ENTERED AT 21:31:54 ON 04 DEC 2011

L5 STRUCTURE UPLOADED

L6 4 S L5 SSS SAM

L7 150 S L5 SSS FULL

FILE 'CAPLUS, MEDLINE' ENTERED AT 21:32:26 ON 04 DEC 2011

L8 35 S L7



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BIB DATA SHEET

CONFIRMATION NO. 1344

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.		
13/099,671	05/03/2011	514	1623	60137.0034USC1		
APPLICANTS Michael Joseph Sofia, Doylestown, PA; Jinfa Du, New Hope, PA; Peiyuan Wang, Glen Rock, NJ;						
** CONTINUING DATA ***** This application is a CON of 12/053,015 03/21/2008 PAT 7,964,580 which claims benefit of 60/909,315 03/30/2007 and claims benefit of 60/982,309 10/24/2007						
** FOREIGN APPLICATIONS *****						
** IF REQUIRED, FOREIGN FILING LICENSE GRANTED *** SMALL ENTITY ** 05/13/2011						
Foreign Priority claimed ☐ Yes ☒ No 35 USC 119(a-d) conditions met ☐ Yes ☒ No Verified and /PATRICK T LEWIS/ Acknowledged Examiner's Signature		☐ Met after Allowance Initials	STATE OR COUNTRY PA	SHEETS DRAWINGS 0	TOTAL CLAIMS 19	INDEPENDENT CLAIMS 2
ADDRESS MERCHANT & GOULD PC P.O. BOX 2903 MINNEAPOLIS, MN 55402-0903 UNITED STATES						
TITLE NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS						
FILING FEE RECEIVED 3840	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:			☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit		

FORM 1449* INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary)	Docket Number: 60137.0034USC1	Application Number: 13/099,671
	Applicant: Sofia et al	
	Filing Date: May 3, 2011	Group Art Unit: 1623

OTHER DOCUMENTS		
		U.S. Patent No. 7,964,580, which issued from US 12/053,015 – Cover Page and Issued Claims.
		Selected Prosecution Documents from US 12/053,015: (1) June 15, 2010 Restriction Requirement; (2) October 28, 2010 Amendment; (3) January 5, 2011 Notice of Allowance; and (4) April 1, 2011 Amendment.
		US 12/783,680, filed May 20, 2010 – Originally filed claims.
		US 13/076,552, filed March 31, 2011 – Originally filed claims.
		US 12/645,710, filed December 23, 2009 – Originally filed claims.
		U.S. Patent No. 7,429,572, which issued from US 10/828,753 – Cover Page and Issued Claims.
		Selected Prosecution Documents from US 10/828,753: (1) February 26, 2007 Amendment; (2) March 30, 2007 Office Action; (3) June 19, 2007 Interview Summary; (4) September 12, 2007 Amendment; (5) September 12, 2007 Declaration; (6) September 24, 2007 Declaration; (7) November 28, 2007 Amendment; (8) February 26, 2008 Office Action; (9) March 11, 2008 Amendment; and (10) May 29, 2008 Notice of Allowance
		US 11/854,218 – Pending Claims as of June 28, 2011
		Selected Prosecution Documents for US 11/854,218: (1) September 12, 2007 Amendment; (2) October 1, 2009 Office Action; (3) March 31, 2010 Response; (4) March 31, 2011 Declaration; (5) July 22, 2010 Office Action; (6) October 11, 2010 Amendment; (7) October 11, 2010 Declaration; (8) December 23, 2010 Office Action; (9) June 28, 2011 Amendment.
		US 12/878,262 – Pending Claims as of September 1, 2011
		Selected Prosecution Documents for US 12/878,262: (1) September 9, 2010 Amendment; (2) June 8, 2011 Office Action; and (3) September 1, 2011 Amendment.

23552 PATENT TRADEMARK OFFICE	
	EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

*Substitute Disclosure Statement Form (PTO-1449)

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /P.L./ (12/04/2011)

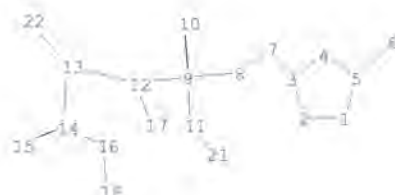
Search Notes 	Application/Control No. 13099671	Applicant(s)/Patent Under Reexamination SOFIA ET AL.
	Examiner PATRICK LEWIS	Art Unit 1623

SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor, REGISTRY, CAPLUS, MEDLINE (see attached)	12/4/2011	/PL/

INTERFERENCE SEARCH			
Class	Subclass	Date	Examiner

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chain nodes :

6 7 8 9 10 11 12 13 14 15 16 17 18 21 22

ring nodes :

1 2 3 4 5

chain bonds :

3-7 5-6 7-8 8-9 9-10 9-11 9-12 11-21 12-13 12-17 13-14 13-22 14-15 14-16 16-18

ring bonds :

1-2 1-5 2-3 3-4 4-5

exact/norm bonds :

1-2 1-5 2-3 3-4 4-5 5-6 7-8 8-9 9-10 9-11 9-12 11-21 12-13 14-15 14-16 16-18

exact bonds :

3-7 12-17 13-14 13-22

G1:CH3,CH2,Et,n-Pr,i-Pr,n-Bu,i-Bu,t-Bu

G2:H,p-C6H4

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 21:CLASS 22:CLASS

FORM 1449* INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary)	Docket Number: 60137.0034USC1	Application Number: 13/099,671
	Applicant: Sofia et al	
	Filing Date: May 3, 2011	Group Art Unit: 1629

U.S. PATENT DOCUMENTS						
EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	6777395	08-17-2004	Bhat			
	6348587	02-19-2002	Schinazi			
	6455513	09-24-2002	McGuigan			
	6812219	11-02-2004	LaColla			
	6911424	06-28-2005	Schinazi			
	6914054	07-05-2005	Sommadossi			
	7018989	03-28-2006	McGuigan			
	7105493	09-12-2006	Sommadossi			
	7105499	09-12-2006	Carroll			
	7125855	10-24-2006	Bhat			
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	7323453	01-29-2008	Olsen			
	7390791	06-24-2008	Becker			
	7429572	09-30-2008	Clark			
	7608597	10-27-2009	Sommadossi			
	7608600	10-27-2009	Storer			
	7635689	12-22-2009	LaColla			
	7879815	02-01-2011	MacCoss			
	20060142238	06-29-2006	McGuigan			
	20070042988	02-22-2007	Klumpp			
	20070197463	08-23-2007	Chun			
	20070265222	11-15-2007	MacCoss			

23552 PATENT TRADEMARK OFFICE	EXAMINER /Patrick Lewis/ (12/04/2011)	DATE CONSIDERED
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

*Substitute Disclosure Statement Form (PTO-1449)

Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /P,L./ (12/04/2011)

FORM 1449* INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary)	Docket Number: 60137.0034USC1	Application Number: 13/099,671
	Applicant: Sofia et al	
	Filing Date: May 3, 2011	Group Art Unit: 1629

	20070275912	11-29-2007	Bhat			
	20100173863	07-08-2010	Schinazi			
	20090306007	12-10-2009	Wagner			
	20100022468	01-08-2010	Meppen			
	20100316594	12-16-2010	Sommadossi			
	20100035835	02-11-2010	Narjes			
	20100152128	06-17-2010	Attenni			
	20110124592	05-26-2011	McGuigan			
			FOREIGN PATENT DOCUMENTS			
	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
	WO2006121820	11-16-2006	PCT			

OTHER DOCUMENTS

	Aquaro et al., Antimicrobial Agents and Chemotherapy (2000) 1: 173-177.
	Chapman et al., Nucleotides, Nucleosides and Nucleic Acids (2001) 20(4-7): 621-628.
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	Eisenberg et al., Nucleosides, Nucleotides & Nucleic Acids (2001) 20(4-7): 1091-1098.
	Lee et al., Antimicrobial Agents and Chemotherapy (2005) 49(5): 1898-1906.
	Ma et al., J. Biol. Chem. (2007) 282(41): 29812-29820.
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	Murakami et al., Antiviral Chemistry & Chemotherapy (2007) 51(2): 503-509.
	Murakami et al., Antimicrobial Agents and Chemotherapy (2008) 52(2): 458-464.
	Perrone et al., J. Med. Chem. (2007) 50(8): 1840-1849.
	Ray et al., Antimicrobial Agents and Chemotherapy (2008) 52(2): 648-654.
	Stuyver et al., Antiviral Chemistry & Chemotherapy (2004) 48(2): 651-654.

23552PATENT TRADEMARK
OFFICE

EXAMINER

/Patrick Lewis/ (12/04/2011)

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

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Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /P.L./ (12/04/2011)

03956.053800.1

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Patrick T. Lewis
MICHAEL JOSEPH SOFIA ET AL.	)	
	:	Art Unit: 1623
Application No.: 13/099,671	)	
	:	Confirmation No.: 1344
Filed: May 3, 2011	)	
	:	
For: NUCLEOSIDE	)	
PHOSPHORAMIDATE	:	
PRODRUGS	)	

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

REVOCATION AND NEW POWER OF ATTORNEY,
CHANGE OF CORRESPONDENCE ADDRESS AND
STATEMENT UNDER 37 CFR 3.73(B)

Sir:

I hereby revoke all previous powers of attorney given in the above-identified application. I hereby appoint practitioners associated with the Customer Number provided below to prosecute the application identified above and to transact all business in the Patent and Trademark Office connected therewith. Please change the correspondence address for the above-identified application to the address associated with the Customer Number provided below.

Fitzpatrick Cella Harper & Scinto (Gilead)

Customer Number: 104538
1290 Avenue of the Americas
New York, New York 10104-3800
Telephone: (212) 218-2100
Facsimile: (212) 218-2200

STATEMENT UNDER 37 C.F.R. 3.73(B)

Gilead Pharmasset LLC, a corporation duly organized under the laws of Delaware, states that it is the assignee of the entire right, title and interest in the patent application identified above by virtue of an assignment in the patent application identified above from the inventors to Pharmasset, Inc. and by virtue of a name change and conversion from Pharmasset, Inc. to Gilead Pharmasset LLC. The assignment was recorded in the United States Patent and Trademark Office at Reel 020739, Frame 0883. The name change and conversion was recorded in the United States Patent and Trademark Office at Reel 028081, Frame 0686.

The undersigned is authorized to act on behalf of the assignee.

Date: 4-23-12 Signature: 
Eric Voelk
Senior Counsel, Intellectual Property
Gilead Pharmasset LLC

FITZPATRICK, CELLA, HARPER & SCINTO
1290 Avenue of the Americas
New York, New York 10104-3800
Facsimile: (212) 218-2200

FCBS_WS 7658029v1.doc

Electronic Acknowledgement Receipt	
EFS ID:	12612242
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	23552
Filer:	Elizabeth F. Holowacz/DAVID NGUY
Filer Authorized By:	Elizabeth F. Holowacz
Attorney Docket Number:	60137.0034USC1
Receipt Date:	24-APR-2012
Filing Date:	03-MAY-2011
Time Stamp:	12:17:16
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	Power of Attorney	039560538001poa.pdf	113463 00009862323181P9028b51d061f4465920f1400b	no	2

Warnings:

Information:

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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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/099,671	05/03/2011	Michael Joseph Sofia	60137.0034USC1

104538
Fitzpatrick Cella Harper & Scinto (Gilead)
1290 Avenue of the Americas
New York, NY 10104

CONFIRMATION NO. 1344
POA ACCEPTANCE LETTER



Date Mailed: 05/01/2012

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/24/2012.

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.

/ddinh/

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



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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/099,671	05/03/2011	Michael Joseph Sofia	60137.0034USC1

23552
MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

CONFIRMATION NO. 1344
POWER OF ATTORNEY NOTICE



Date Mailed: 05/01/2012

NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/24/2012.

- The Power of Attorney to you in this application has been revoked by the assignee who has intervened as provided by 37 CFR 3.71. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

/ddinh/

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

In re Application of:	)	
	:	Examiner: Lewis, Patrick T
MICHAEL JOSEPH SOFIA ET AL.	)	
	:	Group Art Unit: 1623
Application No.: 13/099,671	)	
	:	Confirmation No.: 1344
Filed: May 3, 2011	)	
	:	
For: NUCLEOSIDE	)	
PHOSPHORAMIDATE	:	
PRODRUGS	)	
	:	May 31, 2012

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

AMENDMENT AND RESPONSE
AND PETITION FOR EXTENSION OF TIME

Sir:

Applicants respond to the Office Action dated December 5, 2011. Applicants hereby petition for an extension of time of three months to respond, up through and including June 5, 2012. The extension fee of \$1,270.00 has been paid herewith. Please charge any additional fee required for the extension or credit any overpayment to Deposit Account 50-3939.

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

Amendments to the Claims begin on page 3 of this paper.

Remarks begin on page 22 of this paper.

Amendments to the Specification:

Please amend the paragraph introduced by way of the Preliminary Amendment filed May 3, 2011, after the title but before the sub-heading "Field of Invention" at page 1 as follows:

This application is a continuation of U.S. Patent Application No. 12/053,015, filed March 21, 2008, now U.S. Patent No. 7,964,580, hereby incorporated by reference, which claims priority to U.S. Provisional Patent Application Nos. 60/909,315, filed March 30, 2007, and US 60/982,309, filed October 24, 2007.

Amendments to the Claims:

The following listing of the claims replaces all prior versions and listings.

1.-14. (Canceled).

15. (Previously Presented): A compound selected from among

(S)-methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)acetate;
methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)acetate;
(S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((S)-(4-chlorophenoxy)(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((R)-(4-chlorophenoxy)(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)phosphoryl)amino)propanoate;
(S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate; and

(S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

16. (Previously Presented): The compound of claim 15 selected from among
(S)-methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate; and
(S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

17. (Previously Presented): The compound of claim 15 selected from among
(S)-isopropyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

18. (Previously Presented): The compound of claim 15 selected from among
(S)-methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate
and

(S)-methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

19. (Previously Presented): The compound of claim 18 selected from among
(S)-methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

20. (Previously Presented): The compound of claim 18 selected from among

(S)-methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

21. (Previously Presented): The compound of claim 15 selected from among (S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate; and

(S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

22. (Previously Presented): The compound of claim 21 selected from among (S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

23. (Currently Amended): The compound of claim ~~[[22]]~~21 selected from among (S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

24. (Currently Amended): A pharmaceutical composition comprising the compound ~~or a stereoisomer thereof as claimed in~~ according to any one of claim ~~[[s]] 2 and 13-23~~15.

25. (Currently Amended): ~~[[A]]The pharmaceutical composition according to claim 24comprising the compound or a stereoisomer thereof as claimed in any ones of claims 2 and 13-23 and further comprising a pharmaceutically acceptable medium.~~

26. (Currently Amended): ~~[[A]]The pharmaceutical composition according to claim 25for treating a hepatitis C virus infection, which comprises comprising an effective amount of the compound or a stereoisomer thereof as claimed in~~ according to any one of claim ~~[[s]] 2 and 13-23~~15 and a pharmaceutically acceptable medium to treat a hepatitis C virus infection.

27. (Currently Amended): A method of treating a subject infected by a virus selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus, which comprises ~~[[.]]~~ administering to the subject an effective amount of the compound according to claim 15. ~~[[.]]~~

~~administering to the subject an effective amount of the compound or a stereoisomer thereof as claimed in any one of claims 2 and 13-23;~~

~~wherein the virus is selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus.~~

28. (Canceled).

29. (Currently Amended): ~~[[A]]The method of claim 27 treating a~~ wherein the virus is hepatitis C virus infection in a subject in need thereof, which comprises:

~~administering to the subject an effective amount of the compound as claimed in any one of claims 15-23.~~

30. (Previously presented): The method of claim 29, which further comprises administering to the subject an effective amount of another antiviral agent.

31. (New): A compound or its stereoisomer thereof selected from among

(S)-2-~~[[~~(2R,3R,4R,5R)-5-(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;

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

(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;

(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;

(S)-2-~~[[~~(2R,3R,4R,5R)-5-(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;

(S)-2-~~[[~~(2R,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;~~

{[(2R,3R,4R,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;

(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;

(S)-2-[(2R,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;

(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,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;

(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;

(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-{{(2R,3R,4R,5R)-5-(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;

(S)-2-{{[(2R,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;

(S)-2-{{[(2R,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;

(S)-2-{{[(2R,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;

(S)-2-{{[(2R,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;

(S)-2-{{[(2R,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;

(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;

(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;

(S)-2-{{[(2R,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;

(S)-2-{{[(2R,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;

(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;

(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;

(S)-2-[(2R,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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(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;

(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;

(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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(S)-2-[(2R,3R,4R,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;

(S)-2-{[(2R,3R,4R,5R)-5-(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;

(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;

(S)-2-{[(2R,3R,4R,5R)-5-(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;

(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;

(S)-2-{[(2R,3R,4R,5R)-5-(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;

(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;

(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;

(S)-2-{[(2R,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;

(S)-2-{[(2R,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;

(S)-2-{[(2R,3R,4R,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;

(S)-2- {[(2R,3R,4R,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;

(S)-2- {[(2R,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;

(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;

(S)-2- {[(2R,3R,4R,5R)-5-(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;

(S)-2- {[(2R,3R,4R,5R)-5-(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;

(S)-2- {[(2R,3R,4R,5R)-5-(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;

(S)-2- {[(2R,3R,4R,5R)-5-(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;

(S)-2- {[(2R,3R,4R,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;

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

(S)-2- {[(2R,3R,4R,5R)-5-(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-ethyl ester.

32. (New): The compound of claim 31 or its stereoisomer thereof selected from among

(S)-2-{[(2R,3R,4R,5R)-5-(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;

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

(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;

(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;

(S)-2-{[(2R,3R,4R,5R)-5-(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;

{[(2R,3R,4R,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;

(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;

(S)-2-{[(2R,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;

(S)-2-{[(2R,3R,4R,5R)-5-(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;

(S)-2-{[(2R,3R,4R,5R)-5-(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;

(S)-2-[[{(2R,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;

(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;

(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;

(S)-2-[[{(2R,3R,4R,5R)-5-(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;

(S)-2-[[{(2R,3R,4R,5R)-5-(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;

(S)-2-[[{(2R,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;

(S)-2-[[{(2R,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;

(S)-2-[[{(2R,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;

(S)-2-[[{(2R,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;

(S)-2-[[{(2R,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;

(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;

(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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(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;

(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;

(S)-2-[(2R,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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(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;

(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;

(S)-2-((4-chlorophenoxy)-[(2R,3R,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;

(S)-2-(([(2R,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;

(S)-2-(([(2R,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;

(S)-2-(([(2R,3R,4R,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;

(S)-2-(([(2R,3R,4R,5R)-5-(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;

(S)-2-((2-chlorophenoxy)-[(2R,3R,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;

(S)-2-(([(2R,3R,4R,5R)-5-(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;

(S)-2-((2,4-dichlorophenoxy)-[(2R,3R,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;

(S)-2-(([(2R,3R,4R,5R)-5-(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;

(S)-2-((2-chlorophenoxy)-[(2R,3R,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;

(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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(S)-2-[(2R,3R,4R,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;

(S)-2-[(2R,3R,4R,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;

(S)-2-[(2R,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;

(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,3R,4R,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;

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

(S)-2-[[[(2R,3R,4R,5R)-5-(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-ethyl ester.

33. (New): The compound of claim 32 or its stereoisomer thereof selected from among

(S)-2-[[[(2R,3R,4R,5R)-5-(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;

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

(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;

(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;

(S)-2-[[[(2R,3R,4R,5R)-5-(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;

[[[(2R,3R,4R,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;

(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;

(S)-2-[[[(2R,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;

(S)-2-[[[(2R,3R,4R,5R)-5-(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;

(S)-2- {[(2R,3R,4R,5R)-5-(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;

(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;

(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;

(S)-2- {[(2R,3R,4R,5R)-5-(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;

(S)-2- {[(2R,3R,4R,5R)-5-(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;

(S)-2- {[(2R,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;

(S)-2- {[(2R,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;

(S)-2- {[(2R,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;

(S)-2- {[(2R,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;

(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;

(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;

(S)-2-[(2R,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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(S)-2-[(2R,3R,4R,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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,3R,4R,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;

(S)-2-[(2R,3R,4R,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;

(S)-2-[[[(2R,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;

(S)-2-[[[(2R,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;

(S)-2-[[[(2R,3R,4R,5R)-5-(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; and

(S)-2-[[[(2R,3R,4R,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.

34. (New): The compound of claim 33 or its stereoisomer thereof selected from among

(S)-2-[[[(2R,3R,4R,5R)-5-(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;

(S)-2-[[[(2R,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;

(S)-2-[[[(2R,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;

(S)-2-[[[(2R,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;

(S)-2-[[[(2R,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;

(S)-2-[[[(2R,3R,4R,5R)-5-(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; and

(S)-2-[[[(2R,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.

35. (New): A pharmaceutical composition comprising the compound according to claim 31.

36. (New): The pharmaceutical composition according to claim 35 further comprising a pharmaceutically acceptable medium.

37. (New): The pharmaceutical composition according to claim 36 comprising an effective amount of the compound according to claim 31 to treat a hepatitis C virus infection.

38. (New): A method of treating a subject infected by a virus selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus, which comprises administering to the subject an effective amount of the compound according to claim 31.

39. (New): The method of claim 38 wherein the virus is hepatitis C virus.

40. (New): The method of claim 39, which further comprises administering to the subject an effective amount of another antiviral agent.

REMARKS

The present application has been reviewed in light of the Office Action dated December 5, 2011. Applicants thank the Examiner for the courtesies extended during an interview with Applicants' attorneys on May 24, 2012.

The Specification is amended to show that U.S. Patent Application No. 12/053,015 issued as U.S. Patent No. 7,964,580.

Claims 2, 13 and 14 have been cancelled. New claims 31-40 have been added. Upon entry of the preceding amendment, claims 15-27 and 29-40 will be pending. No new matter has been added by the new and amended claims.

Applicants thank the Examiner for indicating that previously presented claims 15-23 have been allowed. Applicants have amended claim 23 to correct a clerical error in its dependency such that amended claim 23 depends from claim 21 instead of claim 22.

Previously presented claims 24-30 have been amended, *inter alia*, to rely on allowed claims 15-23.

New claims 31-33 correspond to previously presented claims 2, 13 and 14, respectively. Applicants discussed in a May 24, 2012 telephone call with the Examiner that the previously presented claims contained certain clerical errors the correction of which would be difficult to show by amending the previously presented claims. In particular, several of the previously presented claims contained clerical errors in the type of brackets (square brackets [] versus curly braces {}) used in some of the chemical names. Per the May 24, 2012 telephone call with the Examiner, Applicants have cancelled claims 2, 13 and 14 containing the clerical errors and replaced them with new claims 31-33, respectively.

New claim 31 corresponds to previously presented claim 2 with the following changes: square brackets have been changed to curly braces in the 6th, 9th, 13th, 18th-22nd, 26th, 29th, 44th, 45th and 48th chemical names recited in the claim; additionally, the last two compounds recited in claim 31 are newly added to the claim as compared to previously presented claim 2. These additional two compounds recited in claim 31 find support in the specification at pages 666 (Example 48) and 667-668 (Example 60) and do not constitute new matter.

New claim 32 corresponds to previously presented claim 13 with the following changes: square brackets have been changed to curly braces for the 11th, 16th-20th, 24th, 27th and 46th chemical names recited in the claim; three compounds recited in previously presented claim 13 have been deleted from the listing in new claim 32; and the 8th and last two compounds recited in claim 32 are newly added to claim 32 as compared to previously presented claim 13. The 8th compound recited in claim 32 is the same as a compound recited in previously presented claim 2, from which previously presented claim 13 depended. This compound has also been included in new claim 32. The last two compounds recited in new claim 32 are the same as the two additional compounds recited in new claim 31 as compared to original claim 2 (i.e., the last two compounds recited in new claim 31). Support for these two compounds is found at pages 666 (Example 48) and 667-668 (Example 60) of the specification.

New claim 33 corresponds to previously presented claim 14 with the following changes: square brackets have been changed to curly braces for the 21st chemical name recited in the claim; three compounds recited in previously presented claim 14 have been deleted from the listing in new claim 33; and the 8th and 15th-17th compounds recited in new claim 33 are newly added to claim 33 as compared to previously presented claim 14. The 8th and 15th-17th

compounds recited in claim 33 are the same as compounds recited in previously presented claim 2, from which previously presented claim 14 depended indirectly.

New claim 34 corresponds to a subset of compounds that were recited in previously presented claim 2.

Accordingly, only the following two compounds (recited in new claims 31 and 32) were not presented in the previous set of claims:

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

(S)-2-{[(2R,3R,4R,5R)-5-(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-ethyl ester.

As noted above, support for these compounds can be found, for example, in Examples 48 and 60 on pages 666-668 of the specification.

Support for new claims 35-40 is found, for example, in the original claims and on pages 641-649 of the specification.

Claim Rejections Under the Doctrine of Non-Statutory Double Patenting

The Office rejected previously presented claims 2, 13-14 and 24-30 as being unpatentable under the judicially created doctrine of non-statutory double patenting over claims 1-14 of U.S. Patent No. 7,964,580. Previously presented claims 2 and 13-14 have been cancelled and previously presented claims 24-30 have been amended.

In order to advance prosecution of the present application, Applicants respectfully request that the Office enter the concurrently filed Terminal Disclaimer over U.S. Patent No.

7,964,580. The Applicants respectfully request withdrawal of the non-statutory double patenting rejection upon entry of the Terminal Disclaimer.

Request for Correction of Inventorship

Applicants filed, on June 17, 2011, a Rule 48(b) – Request for Correction of Inventorship deleting Dhanapalan Nagarathnam as an inventor. Applicants respectfully request that the Office acknowledge that the inventorship of the application has been corrected and that it has been changed as requested.

Conclusion

In view of the foregoing amendments and remarks, the Applicants assert that all the claims of the present application are patentable. Accordingly, favorable reconsideration of the application is earnestly solicited.

Applicants' undersigned attorneys may be reached in their New York office by telephone at (212) 218-2100. All correspondence should be directed to the address given below.

Respectfully submitted,

/Alicia A. Russo/
Alicia A. Russo
Registration No.: 46,192

Erin J.D. Austin
Registration No.: 66,532

Attorneys for Applicants

FITZPATRICK, CELLA, HARPER & SCINTO
1290 Avenue of the Americas
New York, New York 10104
Facsimile: (212) 218-2200

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
MICHAEL JOSEPH SOFIA ET AL.	)	Examiner: Lewis, Patrick
Application No.: 13/099,671	)	Group Art Unit: 1623
Filed: May 3, 2011	)	
For: NUCLEOSIDE PHOSPHORAMIDATE	)	Date: May 31, 2012
PRODRUGS	)	

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

TERMINAL DISCLAIMER

Sir:

Your petitioner, Gilead Pharmasset LLC, a limited liability corporation duly organized under the laws of Delaware, having a place of business at 303-A College Road East, Princeton, NJ 08540, and duly represented by the undersigned attorneys of record, represents that it is the assignee of the full title and interest in and to the above-identified Application No. 13/099,671, filed May 3, 2011, as evidenced by the deed of Assignment recorded on April 1, 2008 at Reel 020739, Frame 0883 and the change of name recorded on April 20, 2012 at Reel 028081, Frame 0686.

Your petitioner further represents that it is the assignee of the full title and interest in and to U.S. Patent No. 7,964,580, filed on March 21, 2008, as evidenced by the deed of Assignment recorded on April 1, 2008 at Reel 020739, Frame 0883 and the change of name recorded on April 20, 2012 at Reel 02081, Frame 0686.

Your petitioner hereby disclaims the terminal part of any patent granted on the above-identified application which would extend beyond the expiration date of the full statutory term of U.S. Patent No. 7,964,580, as presently shortened by any terminal disclaimer, and hereby agrees that any patent so granted on the above-identified application shall be enforceable only for and during such period that the legal title to said patent shall be the same as the legal title to U.S. Patent No. 7,964,580, this agreement to run with any patent granted on the above-identified application and to be binding upon the grantee, its successors or assigns.

Your petitioner does not disclaim any terminal part of any patent granted on the above-identified application prior to the expiration date of the full statutory term of U.S. Patent No. 7,964,580, as presently shortened by any terminal disclaimer, in the event that subsequent hereto U.S. Patent No. 7,964,580 expires for failure to pay a maintenance fee, is held unenforceable, is found invalid, is the subject of any disclaimer under 37 C.F.R. 1.321(a), has all claims cancelled by a reexamination certificate or is otherwise terminated prior to the expiration of its statutory term as presently shortened by any terminal disclaimer, except for the separation of legal title stated above.

Petitioner's undersigned attorneys may be reached in their New York office by telephone at (212) 218-2100. All correspondence should be directed to the address given below.

Respectfully submitted,

/Alicia A. Russo/
Alicia A. Russo
Registration No.: 46,192

Erin J.D. Austin
Registration No.: 66,532

Attorneys for Applicants

FITZPATRICK, CELLA, HARPER & SCINTO
1290 Avenue of the Americas
New York, New York 10104-3800
Facsimile: (212) 218-2200

Electronic Patent Application Fee Transmittal				
Application Number:		13099671		
Filing Date:		03-May-2011		
Title of Invention:		NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS		
First Named Inventor/Applicant Name:		Michael Joseph Sofia		
Filer:		Erin Julia Daida Austin		
Attorney Docket Number:		03956.053800.1		
Filed as Large Entity				
Utility under 35 USC 111(a) Filing Fees				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension -3 months with \$0 paid	1253	1	1270	1270

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Statutory or terminal disclaimer	1814	1	160	160
Total in USD (\$)				1430

Electronic Acknowledgement Receipt	
EFS ID:	12906804
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	104538
Filer:	Erin Julia Daida Austin/DAVID NGUY
Filer Authorized By:	Erin Julia Daida Austin
Attorney Docket Number:	03956.053800.1
Receipt Date:	31-MAY-2012
Filing Date:	03-MAY-2011
Time Stamp:	17:39:58
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$ 1430
RAM confirmation Number	5146
Deposit Account	503939
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees) Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)	

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		03956_053800_1_amendment.pdf	1294932 665f9502e2778d51e438055e03a4d030a8e44ac7	yes	25
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Amendment/Req. Reconsideration-After Non-Final Reject		1	1	
	Specification		2	2	
	Claims		3	21	
	Applicant Arguments/Remarks Made in an Amendment		22	25	
Warnings:					
Information:					
2	Terminal Disclaimer Filed	03956_053800_1_td.pdf	88672 007e13522b8350cc57444ce261146d4d9cdd47	no	2
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	32095 7bf6a0b6dad495a29a39243961ed594c0cc465b9	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			1415699		

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.

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 13/099,671		Filing Date 05/03/2011		☐ To be Mailed	
APPLICATION AS FILED – PART I										
(Column 1)			(Column 2)			SMALL ENTITY ☒		OR OTHER THAN SMALL ENTITY		
FOR	NUMBER FILED	NUMBER EXTRA	RATE (\$)	FEE (\$)		RATE (\$)	FEE (\$)			
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A				
☐ SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A			N/A				
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A				
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X \$ =			OR	X \$ =			
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X \$ =				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 \$250 (\$125 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			TOTAL				
APPLICATION AS AMENDED – PART II										
(Column 1)			(Column 2)			(Column 3)			SMALL ENTITY OR OTHER THAN SMALL ENTITY	
AMENDMENT	05/31/2012	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)		RATE (\$)	ADDITIONAL FEE (\$)
	Total (37 CFR 1.16(i))	+ 25	Minus	** 88	= 0	X \$30 =	0		OR	X \$ =
	Independent (37 CFR 1.16(h))	+ 2	Minus	*** 3	= 0	X \$125 =	0		OR	X \$ =
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))									
						TOTAL ADD'L FEE	0		OR	TOTAL ADD'L FEE
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)		RATE (\$)	ADDITIONAL FEE (\$)
	Total (37 CFR 1.16(i))	+	Minus	**	=	X \$ =			OR	X \$ =
	Independent (37 CFR 1.16(h))	+	Minus	***	=	X \$ =			OR	X \$ =
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))									
						TOTAL ADD'L FEE			OR	TOTAL ADD'L FEE
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3. ** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20". *** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3". The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.										

Legal Instrument Examiner:
/KIMBERLY WHITE/

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

Application Number 	Application/Control No. 13/099,671	Applicant(s)/Patent under Reexamination SOFIA ET AL.
Document Code - DISQ		Internal Document – DO NOT MAIL

TERMINAL DISCLAIMER	☒ APPROVED	☐ DISAPPROVED
Date Filed : 05/31/12	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by:
Angie Walker

U.S. Patent and Trademark Office



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

NOTICE OF ALLOWANCE AND FEE(S) DUE

104538 7590 06/12/2012
Fitzpatrick Cella Harper & Scinto (Gilead)
1290 Avenue of the Americas
New York, NY 10104

EXAMINER

LEWIS, PATRICK T

ART UNIT PAPER NUMBER

1623

DATE MAILED: 06/12/2012

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/099,671	05/03/2011	Michael Joseph Sofia	03956.053800.1	1344

TITLE OF INVENTION: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

APPL. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$870	\$300	\$0	\$1170	09/12/2012

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 SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

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)

104538 7590 06/12/2012
 Fitzpatrick Cella Harper & Scinto (Gilead)
 1290 Avenue of the Americas
 New York, NY 10104

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.
13/099,671	05/03/2011	Michael Joseph Sofia	03956.053800.1	1344

TITLE OF INVENTION: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$870	\$300	\$0	\$1170	09/12/2012

EXAMINER	ART UNIT	CLASS-SUBCLASS
LEWIS, PATRICK T	1623	514-043000

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 credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

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

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____
 Typed or printed name _____ Registration No. _____

This collection of information 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.



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.
13/099,671	05/03/2011	Michael Joseph Sofia	03956.053800.1	1344

104538 7590 06/12/2012
Fitzpatrick Cella Harper & Scinto (Gilead)
1290 Avenue of the Americas
New York, NY 10104

EXAMINER

LEWIS, PATRICK T

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

1623

DATE MAILED: 06/12/2012

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

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.

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. 13/099,671	Applicant(s) SOFIA ET AL.	
	Examiner PATRICK LEWIS	Art Unit 1623	

-- 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 Terminal Disclaimer filed 5/31/2012.
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 15-27 and 29-40.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - 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. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ 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).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892) 2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date <u>12022011</u> 4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material	5. ☐ Notice of Informal Patent Application 6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ 7. ☐ Examiner's Amendment/Comment 8. ☐ Examiner's Statement of Reasons for Allowance 9. ☐ Other _____
--	--

/Patrick T. Lewis/ Primary Examiner, Art Unit 1623	
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Search Notes 	Application/Control No. 13099671	Applicant(s)/Patent Under Reexamination SOFIA ET AL.
	Examiner PATRICK LEWIS	Art Unit 1623

SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor, REGISTRY, CAPLUS, MEDLINE (see attached)	12/4/2011	/PL/
Updated Inventor, REGISTRY, CAPLUS, MEDLINE searches	6/5/2012	/PL/

INTERFERENCE SEARCH			
Class	Subclass	Date	Examiner
514	43, 45, 46, 47, 48, 49, 50, 51	6/5/2012	/PL/

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Issue Classification 	Application/Control No. 13099671	Applicant(s)/Patent Under Reexamination SOFIA ET AL.
	Examiner PATRICK LEWIS	Art Unit 1623

ORIGINAL						INTERNATIONAL CLASSIFICATION												
CLASS		SUBCLASS				CLAIMED					NON-CLAIMED							
514		43				A	0	1	N	42 / 04 (2006 01.01)								
CROSS REFERENCE(S)						A	6	1	K	31 / 70 (2006 01.01)								
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)																	
514	45	46	47	48	49													
514	50	51																

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47															
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
	1		17		33										
	2		18		34										
	3		19		35										
	4		20		36										
	5		21		37										
	6		22		38										
	7		23		39										
	8		24		40										
	9		25												
	10		26												
	11		27												
	12		28												
	13		29												
	14		30												
	15		31												
	16		32												

NONE		Total Claims Allowed:	
		25	
(Assistant Examiner)	(Date)	O.G. Print Claim(s)	O.G. Print Figure
/PATRICK LEWIS/ Primary Examiner, Art Unit 1623	6/5/2012	1	None
(Primary Examiner)	(Date)		

Index of Claims 	Application/Control No. 13099671	Applicant(s)/Patent Under Reexamination SOFIA ET AL.
	Examiner PATRICK LEWIS	Art Unit 1623

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

☒ Claims renumbered in the same order as presented by applicant				☐ CPA				☒ T.D.				☐ R.1.47			
CLAIM		DATE													
Final	Original	12/04/2011	06/05/2012												
	1	-	-												
	2	✓	-												
	3	-	-												
	4	-	-												
	5	-	-												
	6	-	-												
	7	-	-												
	8	-	-												
	9	-	-												
	10	-	-												
	11	-	-												
	12	-	-												
	13	✓	-												
	14	✓	-												
	15	=	=												
	16	=	=												
	17	=	=												
	18	=	=												
	19	=	=												
	20	=	=												
	21	=	=												
	22	=	=												
	23	=	=												
	24	✓	=												
	25	✓	=												
	26	✓	=												
	27	✓	-												
	28	✓	=												
	29	✓	=												
	30	✓	=												
	31		=												
	32		=												
	33		=												
	34		=												
	35		=												
	36		=												

<i>Index of Claims</i> 	Application/Control No. 13099671	Applicant(s)/Patent Under Reexamination SOFIA ET AL.
	Examiner PATRICK LEWIS	Art Unit 1623

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

☒ Claims renumbered in the same order as presented by applicant										☐ CPA										☒ T.D.										☐ R.1.47									
CLAIM		DATE																																					
Final	Original	12/04/2011	06/05/2012																																				
	37		=																																				
	38		=																																				
	39		=																																				
	40		=																																				

FORM 1449* INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary)	Docket Number: 60137.0034USC1	Application Number: 13/099,671
	Applicant: Sofia et al	
	Filing Date: May 3, 2011	Group Art Unit: 1623

OTHER DOCUMENTS		
		~~U.S. Patent No. 7,904,580, which issued from US 12/053,015 - Cover Page and Issued Claims.~~
		Selected Prosecution Documents from US 12/053,015: (1) June 15, 2010 Restriction Requirement; (2) October 28, 2010 Amendment; (3) January 5, 2011 Notice of Allowance; and (4) April 1, 2011 Amendment.
		US 12/783,680, filed May 20, 2010 - Originally filed claims.
		US 13/076,552, filed March 31, 2011 - Originally filed claims.
		US 12/645,710, filed December 23, 2009 - Originally filed claims.
		~~U.S. Patent No. 7,429,572, which issued from US 10/928,753 - Cover Page and Issued Claims.~~
		Selected Prosecution Documents from US 10/828,753: (1) February 26, 2007 Amendment; (2) March 30, 2007 Office Action; (3) June 19, 2007 Interview Summary; (4) September 12, 2007 Amendment; (5) September 12, 2007 Declaration; (6) September 24, 2007 Declaration; (7) November 28, 2007 Amendment; (8) February 26, 2008 Office Action; (9) March 11, 2008 Amendment; and (10) May 29, 2008 Notice of Allowance
		US 11/854,218 - Pending Claims as of June 28, 2011
		Selected Prosecution Documents for US 11/854,218: (1) September 12, 2007 Amendment; (2) October 1, 2009 Office Action; (3) March 31, 2010 Response; (4) March 31, 2011 Declaration; (5) July 22, 2010 Office Action; (6) October 11, 2010 Amendment; (7) October 11, 2010 Declaration; (8) December 23, 2010 Office Action; (9) June 28, 2011 Amendment.
		US 12/878,262 - Pending Claims as of September 1, 2011
		Selected Prosecution Documents for US 12/878,262: (1) September 9, 2010 Amendment; (2) June 8, 2011 Office Action; and (3) September 1, 2011 Amendment.

23552 PATENT TRADEMARK OFFICE	
	EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

EXAMINER

/Patrick Lewis/ (06/06/2012)

DATE CONSIDERED

*Substitute Disclosure Statement Form (PTO-1449)

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /P.L./ (06/06/2012)

WEST Search History

DATE: Tuesday, June 05, 2012

Hide? **Set Name** **Query****Hit Count***Interference**DB=PGPB,USPT; PLUR=YES; OP=ADJ*

☐	L5	L4 and phosphoramidite prodrug	5
☐	L4	L3 and prodrug	134
☐	L3	L1 and phosphoramidite	248
☐	L2	(514/43,45,46,47,48,49,50,51)![CCLS]	5190
☐	L1	(514/43,45,46,47,48,49,50,51)[CCLS]	5190

END OF SEARCH HISTORY



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/099,671	05/03/2011	Michael Joseph Sofia	03956.053800.1	1344

104538 7590 08/27/2012
Fitzpatrick Cella Harper & Scinto (Gilead)
1290 Avenue of the Americas
New York, NY 10104

EXAMINER

LEWIS, PATRICK T

ART UNIT	PAPER NUMBER
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1623

MAIL DATE	DELIVERY MODE
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08/27/2012

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.



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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
13/099,671	03 May, 2011	SOFIA ET AL.	03956.053800.1

Fitzpatrick Cella Harper & Scinto (Gilead) 1290 Avenue of the Americas New York, NY 10104	EXAMINER	
	PATRICK LEWIS	
	ART UNIT	PAPER
	1623	20120823

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

This application currently contains a Request under Rule 48 Correcting Inventorship filed on June 17, 2011. According to applicant's representative, said Request has been submitted in error.

37 CFR 1.59 provides that information, other than the original disclosure of the application, may be expunged from the file wrapper provided a petition to expunge under 37 CFR 1.59(b) and the required fee set forth in 37 CFR 1.17(g) are filed, and further that petitioner has established to the satisfaction of the Director that the return of the information is appropriate. Expungement of information that was originally submitted to the Office under MPEP § 724.02, or that should have been submitted in a sealed envelope as discussed in MPEP § 724.02, is appropriate when the petitioner complies with items (A)-(E) set forth in MPEP § 724.05, paragraph I, and the examiner or other appropriate Office official who is responsible for considering the information has determined that the information is not ** material to patentability *. Expungement of information that was inadvertently submitted to the Office is appropriate provided that items (A)-(F) set forth in MPEP § 724.05, paragraph II, are satisfied. See also MPEP § 724.

Where the information to be expunged was not submitted pursuant to MPEP § 724.02 or as part of an Information Disclosure Statement, the petition should be sent to the Office of Petitions for decision.

/Patrick T. Lewis/
Primary Examiner, Art Unit 1623



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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
13/099,671	05/03/2011	1623	3840	03956.053800.1	19	2

CONFIRMATION NO. 1344

CORRECTED FILING RECEIPT

104538

Fitzpatrick Cella Harper & Scinto (Gilead)
1290 Avenue of the Americas
New York, NY 10104



0000000056228498

Date Mailed: 08/28/2012

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**

Applicant(s)

Michael Joseph Sofia, Doylestown, PA;
Jinfa Du, New Hope, PA;
Peiyuan Wang, Glen Rock, NJ;
Dhanapalan Nagarathnam, Bethany, CT;

Assignment For Published Patent Application

Pharmasset, Inc., Princeton, NJ

Power of Attorney: The patent practitioners associated with Customer Number 104538

Domestic Priority data as claimed by applicant

This application is a CON of 12/053,015 03/21/2008 PAT 7964580
which claims benefit of 60/909,315 03/30/2007
and claims benefit of 60/982,309 10/24/2007

Foreign Applications (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see <http://www.uspto.gov> for more information.)

If Required, Foreign Filing License Granted: 05/13/2011

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 13/099,671**

Projected Publication Date: Not Applicable

Non-Publication Request: No

Early Publication Request: No

**** SMALL ENTITY ****

Title

NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

Preliminary Class

514

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

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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 (1-866-999-4158).

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Lewis, Patrick T
MICHAEL JOSEPH SOFIA ET AL.	)	
	:	Group Art Unit: 1623
Application No.: 13/099,671	)	
	:	Confirmation No.: 1344
Filed: May 3, 2011	)	
	:	
For: NUCLEOSIDE	)	
PHOSPHORAMIDATE	:	
PRODRUGS	)	
	:	September 4, 2012

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

AMENDMENT UNDER 37 C.F.R. § 1.312

Sir:

Applicants are in receipt of a Notice of Allowance and Fee Due dated June 12, 2012. Applicants respectfully request entry of the following amendments. No fee is believed to be due in connection with this paper. However the Commissioner is hereby authorized to charge any fee which may be required in connection with this paper, and to credit any overpayment, to Deposit Account No. 50-3939.

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

Amendments to the Claims begin on page 3 of this paper.

Remarks begin on page 22 of this paper.

Amendments to the Specification:

Please amend the paragraph after the title but before the sub-heading "Field of Invention" at page 1, which was added by a Preliminary Amendment submitted on May 3, 2011, as follows:

This application is a continuation of U.S. Patent Application No. 12/053,015, filed March 21, 2008, ~~hereby incorporated by reference~~, which issued as U.S. Patent No. 7,964,580 on June 21, 2011 and which claims priority to U.S. Provisional Patent Application Nos. 60/909,315 filed March 30, 2007 and [[US]]60/982,309, filed October 24, 2007, all of which are incorporated by reference in their entireties.

Amendments to the Claims:

Please amend Claims 31 and 32 as follows:

1.-14. (Canceled).

15. (Previously Presented): A compound selected from among
(S)-methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)acetate;
methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)acetate;
(S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((S)-(4-chlorophenoxy))(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((R)-(4-chlorophenoxy))(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)phosphoryl)amino)propanoate;
(S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate; and

(S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

16. (Previously Presented): The compound of claim 15 selected from among
(S)-methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-isopropyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate;
(S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate; and
(S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

17. (Previously Presented): The compound of claim 15 selected from among
(S)-isopropyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

18. (Previously Presented): The compound of claim 15 selected from among
(S)-methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate
and

(S)-methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

19. (Previously Presented): The compound of claim 18 selected from among
(S)-methyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

20. (Previously Presented): The compound of claim 18 selected from among

(S)-methyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate.

21. (Previously Presented): The compound of claim 15 selected from among

(S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate; and

(S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

22. (Previously Presented): The compound of claim 21 selected from among

(S)-cyclohexyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

23. (Previously Presented): The compound of claim 21 selected from among

(S)-cyclohexyl 2-(((R)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(4-fluorophenoxy)phosphoryl)amino)propanoate.

24. (Previously Presented): A pharmaceutical composition comprising the compound according to claim 15.

25. (Previously Presented): The pharmaceutical composition according to claim 24 further comprising a pharmaceutically acceptable medium.

26. (Previously Presented): The pharmaceutical composition according to claim 25 comprising an effective amount of the compound according to claim 15 to treat a hepatitis C virus infection.

27. (Previously Presented): A method of treating a subject infected by a virus selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus, which comprises administering to the subject an effective amount of the compound according to claim 15.

28. (Canceled).

29. (Previously Presented): The method of claim 27 wherein the virus is hepatitis C virus.

30. (Previously presented): The method of claim 29, which further comprises administering to the subject an effective amount of another antiviral agent.

31. (Currently Amended): A compound or its stereoisomer thereof selected from among

(S)-2-([(2R,3R,4R,5R)-5-(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;

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

(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;

(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,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;

{[(2R,3R,4R,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;

(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;

(S)-2-([(2R,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;

(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;

(S)-2-[[[(2R,3R,4R,5R)-5-(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;

(S)-2-[[[(2R,3R,4R,5R)-5-(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;

(S)-2-[[[(2R,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;

(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;

(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;

(S)-2-[[[(2R,3R,4R,5R)-5-(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;

(S)-2-[[[(2R,3R,4R,5R)-5-(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;

(S)-2-[[[(2R,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;

(S)-2-[[[(2R,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;

(S)-2-([(2R,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;

(S)-2-([(2R,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;

(S)-2-([(2R,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;

(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;

(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;

(S)-2-([(2R,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;

(S)-2-([(2R,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;

(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;

(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;

(S)-2-([(2R,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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(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}-propionic acid isopropyl ester;

(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;

(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;

(S)-2-([(2R,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;

(S)-2-([(2R,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;

(S)-2-([(2R,3R,4R,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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

~~(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;~~

(S)-2-([(2R,3R,4R,5R)-5-(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;

(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(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;

(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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(S)-2-[(2R,3R,4R,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;

(S)-2-[(2R,3R,4R,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;

(S)-2-[(2R,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;

(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,3R,4R,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;

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

(S)-2-([(2R,3R,4R,5R)-5-(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-ethyl ester.

32. (Currently Amended): The compound of claim 31 or its stereoisomer thereof selected from among

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,3R,4R,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-butyl acid methyl ester;

(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;

(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

{[(2R,3R,4R,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;

(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;

(S)-2-[(2R,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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,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;

(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;

(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(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;

(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;

(S)-2-([(2R,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;

(S)-2-([(2R,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;

(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;

(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;

(S)-2-([(2R,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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(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;

(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;

(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;

(S)-2-([(2R,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;

(S)-2-([(2R,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;

(S)-2-([(2R,3R,4R,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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(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;

(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;

(S)-2-([(2R,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;

(S)-2-([(2R,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;

(S)-2-([(2R,3R,4R,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;

(S)-2-([(2R,3R,4R,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;

(S)-2-([(2R,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;

(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,3R,4R,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;

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

(S)-2-([(2R,3R,4R,5R)-5-(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-ethyl ester.

33. (Previously Presented): The compound of claim 32 or its stereoisomer thereof selected from among

(S)-2-([(2R,3R,4R,5R)-5-(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;

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

(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;

(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

([(2R,3R,4R,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;

(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;

(S)-2-([(2R,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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(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;

(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,3R,4R,5R)-5-(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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(S)-2-[(2R,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;

(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;

(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;

(S)-2-([(2R,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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,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;

(S)-2-([(2R,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;

(S)-2-([(2R,3R,4R,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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,3R,4R,5R)-5-(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;

(S)-2-([(2R,3R,4R,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;

(S)-2-([(2R,3R,4R,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;

(S)-2-([(2R,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;

(S)-2-{[(2R,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;

(S)-2-{[(2R,3R,4R,5R)-5-(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; and

(S)-2-{[(2R,3R,4R,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.

34. (Previously Presented): The compound of claim 33 or its stereoisomer thereof selected from among

(S)-2-{[(2R,3R,4R,5R)-5-(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;

(S)-2-{[(2R,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;

(S)-2-{[(2R,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;

(S)-2-{[(2R,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;

(S)-2-{[(2R,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;

(S)-2-{[(2R,3R,4R,5R)-5-(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; and

(S)-2-{[(2R,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.

35. (Previously Presented): A pharmaceutical composition comprising the compound according to claim 31.

36. (Previously Presented): The pharmaceutical composition according to claim 35 further comprising a pharmaceutically acceptable medium.

37. (Previously Presented): The pharmaceutical composition according to claim 36 comprising an effective amount of the compound according to claim 31 to treat a hepatitis C virus infection.

38. (Previously Presented): A method of treating a subject infected by a virus selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus, which comprises administering to the subject an effective amount of the compound according to claim 31.

39. (Previously Presented): The method of claim 38 wherein the virus is hepatitis C virus.

40. (Previously Presented): The method of claim 39, which further comprises administering to the subject an effective amount of another antiviral agent.

REMARKS

Applicants thank the Examiner for the Office Communication mailed August 27, 2012, and the Corrected Filing Receipt mailed August 28, 2012. A separate Petition to Expunge Under 37 C.F.R. § 1.59 is submitted concurrently pursuant to the Office Communication mailed August 27, 2012.

The first sentence of the specification, which was added by a Preliminary Amendment submitted on May 3, 2011, is amended to state that U.S. Application No. 12/053,015, filed March 21, 2008, issued as U.S. Patent No. 7,964,580 on June 21, 2011, and to clarify that the present application incorporates by reference in their entireties all of the U.S. provisional and non-provisional applications to which it claims priority.

Claims 31 and 32 are presently amended to delete in each claim one instance of a chemical name that is recited twice.

It is respectfully submitted that these amendments are merely corrections of formal matters, do not change the scope of the claims, and will not require a substantial amount of additional work on the part of the Office. MPEP 714.16. Favorable consideration and entry hereof is respectfully requested.

Applicants' undersigned attorneys may be reached in their New York office by telephone at (212) 218-2100. All correspondence should be directed to the address given below.

Respectfully submitted,

/Alicia A. Russo/

Alicia A. Russo
Registration No.: 46,192

Erin J.D. Austin
Registration No.: 66,532

Attorneys for Applicants

FITZPATRICK, CELLA, HARPER & SCINTO
1290 Avenue of the Americas
New York, New York 10104
Facsimile: (212) 218-2200

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Lewis, Patrick T
MICHAEL JOSEPH SOFIA ET AL.	)	
	:	Group Art Unit: 1623
Application No.: 13/099,671	)	
	:	Confirmation No.: 1344
Filed: May 3, 2011	)	
	:	
For: NUCLEOSIDE	)	
PHOSPHORAMIDATE	:	
PRODRUGS	)	
	:	September 4, 2012

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

PETITION TO EXPUNGE UNDER 37 C.F.R. § 1.59

Sir:

In accordance with 37 C.F.R. § 1.59, Applicants respectfully request that the Rule 48(b) – Request for Correction of Inventorship submitted on June 17, 2011, be expunged from the above-captioned application. The Rule 48(b) – Request for Correction of Inventorship was erroneously submitted, as noted in the Official Communication mailed August 27, 2012. Applicants also request that Applicants' following Remarks regarding the June 17, 2011, Rule 48(b) – Request for Correction of Inventorship likewise be expunged from the record of the above-captioned application: (1) Second Preliminary Amendment submitted on June 17, 2011, p. 17, lns. 11-13; and (2) Amendment and Response and Petition for Extension of Time submitted on May 31, 2012, p. 25, lns. 3-7.

A petition fee of \$200.00 pursuant to 37 C.F.R. § 1.17(g) is paid concurrently herewith. Any additional fees deemed necessary may be deducted from Deposit Account No. 50-3939.

Applicants' undersigned attorneys may be reached in their New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to the address given below.

Respectfully submitted,

/Alicia A. Russo/

Alicia A. Russo
Registration No.: 46,192

Erin J.D. Austin
Registration No.: 66,532

Attorneys for Applicants

FITZPATRICK, CELLA, HARPER & SCINTO
1290 Avenue of the Americas
New York, New York 10104
Facsimile: (212) 218-2200

Electronic Patent Application Fee Transmittal				
Application Number:	13099671			
Filing Date:	03-May-2011			
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS			
First Named Inventor/Applicant Name:	Michael Joseph Sofia			
Filer:	Erin Julia Daida Austin/Wendy Valdez			
Attorney Docket Number:	03956.053800.1			
Filed as Large Entity				
Utility under 35 USC 111(a) Filing Fees				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Petition fee- 37 CFR 1.17(g) (Group II)	1463	1	200	200
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Total in USD (\$)				200

Electronic Acknowledgement Receipt	
EFS ID:	13650348
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	104538
Filer:	Erin Julia Daida Austin/DAVID NGUY
Filer Authorized By:	Erin Julia Daida Austin
Attorney Docket Number:	03956.053800.1
Receipt Date:	04-SEP-2012
Filing Date:	03-MAY-2011
Time Stamp:	15:00:16
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$ 200
RAM confirmation Number	1547
Deposit Account	503939
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees) Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)	

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		039560538001_312Amendment.pdf	122847 42660c714937175a783c117e0f0b12106ade34b60	yes	23
	Multipart Description/PDF files in .zip description				
	Document Description		Start		End
	Amendment after Notice of Allowance (Rule 312)		1		1
	Specification		2		2
	Claims		3		21
	Applicant Arguments/Remarks Made in an Amendment		22		23
Warnings:					
Information:					
2	Miscellaneous Incoming Letter	039560538001_PetitionToExpu nge.pdf	80778 396c9932 b6b9a6396c545ec0a6f60a3a1c1e18	no	2
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30464 10f0314562900db0c2c9c1000c70e32a31bd194e78	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			234089		

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.

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)

104538 7590 06/12/2012
 Fitzpatrick Cella Harper & Scinto (Gilead)
 1290 Avenue of the Americas
 New York, NY 10104

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.
13/099,671	05/03/2011	Michael Joseph Sofia	03956.053800.1	1344

TITLE OF INVENTION: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$870	\$300	\$0	\$1170	09/12/2012

EXAMINER	ART UNIT	CLASS-SUBCLASS
LEWIS, PATRICK T	1623	514-043000

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 Fitzpatrick, Cella, Harper
 & Scinto

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

Gilead Pharmasset LLC

(B) RESIDENCE: (CITY AND STATE OR COUNTRY)

Foster City, CA

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 credit any overpayment, to Deposit Account Number 50-3939 (enclose an extra copy of this form).

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

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☒ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature /Alicia A. Russo/

Date September 11, 2012

Typed or printed name Alicia A. Russo

Registration No. 46,192

This collection of information 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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Lewis, Patrick T
MICHAEL JOSEPH SOFIA ET AL.	)	
	:	Group Art Unit: 1623
Application No.: 13/099,671	)	
	:	Confirmation No.: 1344
Filed: May 3, 2011	)	
	:	
For: NUCLEOSIDE	)	
PHOSPHORAMIDATE	:	
PRODRUGS	)	
	:	September 11, 2012

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

NOTIFICATION OF LOSS OF ENTITLEMENT TO SMALL ENTITY STATUS

Sir:

Applicants hereby notify the Office pursuant to 37 C.F.R. § 1.27(g) that there has been a loss of entitlement to small entity status in the above-identified application. Accordingly, Applicants concurrently pay the non-small entity issue fee due on September 12, 2012. The Commissioner is authorized to credit any overpayment or charge any deficiency in this payment to Deposit Account 50-3939.

Applicants' undersigned attorneys may be reached in their New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to the address given below.

Respectfully submitted,

/Alicia A. Russo/

Alicia A. Russo
Registration No.: 46,192

Erin J.D. Austin
Registration No.: 66,532

Attorneys for Applicants

FITZPATRICK, CELLA, HARPER & SCINTO
1290 Avenue of the Americas
New York, New York 10104
Facsimile: (212) 218-2200

Electronic Patent Application Fee Transmittal				
Application Number:		13099671		
Filing Date:		03-May-2011		
Title of Invention:		NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS		
First Named Inventor/Applicant Name:		Michael Joseph Sofia		
Filer:		Erin Julia Daida Austin/Maria Miglio		
Attorney Docket Number:		03956.053800.1		
Filed as Large Entity				
Utility under 35 USC 111(a) Filing Fees				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Utility Appl issue fee	1501	1	1740	1740
Publ. Fee- early, voluntary, or normal	1504	1	300	300

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				2040

Electronic Acknowledgement Receipt	
EFS ID:	13710811
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	104538
Filer:	Erin Julia Daida Austin/DAVID NGUY
Filer Authorized By:	Erin Julia Daida Austin
Attorney Docket Number:	03956.053800.1
Receipt Date:	11-SEP-2012
Filing Date:	03-MAY-2011
Time Stamp:	14:39:18
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$ 2040
RAM confirmation Number	1007
Deposit Account	503939
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees) Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)	

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

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	039560538001-IssueFee.pdf	103733 e4512e24f811b599f11f567c7728b09c051c58	no	1

Warnings:

Information:

2	Miscellaneous Incoming Letter	03956053800-1Notification.pdf	80856 c2e231f26358e0a28f7bd8fa020e2b110b099f	no	2
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Warnings:

Information:

3	Fee Worksheet (SB06)	fee-info.pdf	31956 fe071c7a56d0e258285c53f8f0a0e31f1f0a2d3f	no	2
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Warnings:

Information:

Total Files Size (in bytes):	216545
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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.



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.
13/099,671	05/03/2011	Michael Joseph Sofia	03956.053800.1	1344
104538 7590 10/24/2012 Fitzpatrick Cella Harper & Scinto (Gilead) 1290 Avenue of the Americas New York, NY 10104			EXAMINER LEWIS, PATRICK T	
			ART UNIT 1623	PAPER NUMBER
			MAIL DATE 10/24/2012	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

Fitzpatrick Cella Harper & Scinto (Gilead)
1290 Avenue of the Americas
New York NY 10104

In re Application of:
Sofia et al.
Serial No.: 13/099,671
Filed: May 3, 2011
Attorney Docket No.: 03956.053800.1

OCT 24 2012

PETITION DECISION

This is in response to the petition under 37 CFR § 1.59(b), filed September 4, 2012, to expunge information from the above identified application. This application has been allowed.

Petitioner requests that the Rule 48(b) - Request for Correction of Inventorship submitted on June 17, 2011, be expunged from the above-captioned application. The Rule 48(b) - Request for Correction of Inventorship was erroneously submitted, as noted in the Official Communication mailed August 27, 2012. Applicants also request that Applicants' following Remarks regarding the June 17, 2011, 48(b) - Request for Correction of Inventorship likewise be expunged from the record of the above-captioned application: (1) Second Preliminary Amendment submitted on June 17, 2011, p. 17, Ins. 11-13; and (2) Amendment and Response and Petition for Extension of Time submitted on May 31, 2012, p. 25, Ins. 3-7. Petitioner states either: (A) that the information contains trade secret material, proprietary material and/or material that is subject to a protective order which has not been made public; or (B) that the information submitted was unintentionally submitted and the failure to obtain its return would cause irreparable harm to the party who submitted the information or to the party in interest on whose behalf the information was submitted, and the information has not otherwise been made public. The petition fee set forth in 37 CFR § 1.17(g) has been paid.

The reasons set forth in this petition establishes to the satisfaction of the Director that expungement of the information is appropriate. The file entry for this document has been closed and as such the document is no longer publicly available, which is the IFW equivalent to removal of a paper document from a paper file wrapper.

Therefore, petitioner's petition is GRANTED.

Should there be any questions about this decision please contact Marianne C. Seidel by letter addressed to Director, TC 1600, at the address listed above, or by telephone at 571-272-0584 or by facsimile sent to the general Office facsimile number, 571-273-8300.

/MC Seidel/
Marianne C. Seidel, Quality Assurance Specialist
Technology Center 1600



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

MAILED

OCT 25 2012

OFFICE OF PETITIONS

Fitzpatrick Cella Harper & Scinto (Gilead)
1290 Avenue of the Americas
New York NY 10104

In re Application of :
Michael Joseph Sofia et al. :
Application No. 13/099,671 : **DECISION ON PETITION**
Filed: May 3, 2011 :
Attorney Docket No. 03956.053800.1 :

This is a decision on the Petition to Expunge Under 37 CFR 1.59, filed September 4, 2012, which is being treated as a petition under 37 CFR 1.59(b) to expunge information from the above identified application.

The petition is **dismissed**.

Petitioner requests that the petition under 37 CFR 1.48 and related amendments, filed on June 17, 2011, be expunged from the record. Petitioner requests that the petition under 37 CFR 1.48 to correct inventorship be expunged as it was filed unintentionally.

MPEP 724.05(II) states in part:

II. INFORMATION UNINTENTIONALLY SUBMITTED IN APPLICATION

A petition to expunge information unintentionally submitted in an application (other than information forming part of the original disclosure) may be filed under 37 CFR 1.59(b), provided that:

- (A) the Office can effect such return prior to the issuance of any patent on the application in issue;
- (B) it is stated that the information submitted was unintentionally submitted and the failure to obtain its return would cause irreparable harm to the party who submitted the information or to the party in interest on whose behalf the information was submitted;
- (C) the information has not otherwise been made public;
- (D) there is a commitment on the part of the petitioner to retain such information for the period of any patent with regard to which such information is submitted;

The petition is deficient because there is no statement addressing (B) (C) and (D).

Further, petitioner characterizes the petition under 37 CFR 1.48 as filed unintentionally. However, at the time the petition under 37 CFR 1.48 was filed, clearly applicants determined, erroneously or not, that one of the listed co-inventors should be deleted. Therefore, the petition under 37 CFR 1.48 was intentionally filed and expungement is not the procedure for removing the petition.

Petitioner should file a petition to **withdraw** the 37 CFR 1.48 petition. This petition should be directed to the Director, Technology Center 1600.

Telephone inquiries concerning this communication should be directed to Carl Friedman at (571) 272-6842.



Carl Friedman
Petitions Examiner
Office of Petitions

OK TO ENTER: /P.L./ (11/03/2012)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Lewis, Patrick T
MICHAEL JOSEPH SOFIA ET AL.	)	
	:	Group Art Unit: 1623
Application No.: 13/099,671	)	
	:	Confirmation No.: 1344
Filed: May 3, 2011	)	
	:	
For: NUCLEOSIDE	)	
PHOSPHORAMIDATE	:	
PRODRUGS	)	
	:	September 4, 2012

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

AMENDMENT UNDER 37 C.F.R. § 1.312

Sir:

Applicants are in receipt of a Notice of Allowance and Fee Due dated June 12, 2012. Applicants respectfully request entry of the following amendments. No fee is believed to be due in connection with this paper. However the Commissioner is hereby authorized to charge any fee which may be required in connection with this paper, and to credit any overpayment, to Deposit Account No. 50-3939.

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

Amendments to the Claims begin on page 3 of this paper.

Remarks begin on page 22 of this paper.



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.
13/099,671	05/03/2011	Michael Joseph Sofia	03956.053800.1	1344

104538 7590 11/06/2012
Fitzpatrick Cella Harper & Scinto (Gilead)
1290 Avenue of the Americas
New York, NY 10104

EXAMINER

LEWIS, PATRICK T

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

1623

MAIL DATE	DELIVERY MODE
-----------	---------------

11/06/2012

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Response to Rule 312 Communication	Application No. 13/099,671	Applicant(s) SOFIA ET AL.
	Examiner PATRICK LEWIS	Art Unit 1623
<i>– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –</i>		
1. ☒ The amendment filed on <u>04 September 2012</u> under 37 CFR 1.312 has been considered, and has been: a) ☒ entered. b) ☐ entered as directed to matters of form not affecting the scope of the invention. c) ☐ disapproved because the amendment was filed after the payment of the issue fee. Any amendment filed after the date the issue fee is paid must be accompanied by a petition under 37 CFR 1.313(c)(1) and the required fee to withdraw the application from issue. d) ☐ disapproved. See explanation below. e) ☐ entered in part. See explanation below.		
		/Patrick T. Lewis/ Primary Examiner, Art Unit 1623



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.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/099,671	12/18/2012	8334270	03956.053800.1	1344
104538	7590	11/28/2012		
Fitzpatrick Cella Harper & Scinto (Gilead) 1290 Avenue of the Americas New York, NY 10104				

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

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

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

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 Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional applicants):

Michael Joseph Sofia, Doylestown, PA;
Jinfa Du, New Hope, PA;
Peiyuan Wang, Glen Rock, NJ;
Dhanapalan Nagarathnam, Bethany, CT;

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 USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Lewis, Patrick T
MICHAEL JOSEPH SOFIA ET AL.	)	
	:	Group Art Unit: 1623
Application No.: 13/099,671	)	
	:	Confirmation No.: 1344
Filed: May 3, 2011	)	
	:	
For: NUCLEOSIDE	)	
PHOSPHORAMIDATE	:	
PRODRUGS	)	
	:	November 29, 2012

Director, Technology Center 1600
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

**PETITION TO WITHDRAW RULE 48(b) – REQUEST
FOR CORRECTION OF INVENTORSHIP**

Sir:

On September 4, 2012, Applicants submitted a Petition to Expunge Under 37 C.F.R. § 1.59 as suggested in the Office Communication Mailed August 27, 2012. Said petition requested that the Rule 48(b) – Request for Correction of Inventorship submitted on June 17, 2011, as well as Applicants' remarks regarding the Rule 48(b) Request, be expunged from the record of the above-referenced application. The September 4, 2012 Petition to Expunge Under 37 C.F.R. § 1.59 was granted in a Petition Decision mailed October 24, 2012 and denied in a Decision on Petition mailed October 25, 2012. Pursuant to a telephone conversation with the Examiner on November 26, 2012, Applicants understand that said petition has been denied. The

Decision on Petition mailed October 25, 2012 advised Applicants to submit a Petition to Withdraw the Rule 48(b) Request.

Accordingly, pursuant to the Decision on Petition mailed October 25, 2012, and Applicants' telephone conversation with the Examiner on November 26, 2012, Applicants hereby respectfully request that the Rule 48(b) – Request for Correction of Inventorship submitted on June 17, 2011, be withdrawn from the above-captioned application. The Rule 48(b) – Request for Correction of Inventorship was erroneously submitted, as noted in the Official Communication mailed August 27, 2012. Applicants also request that Applicants' following Remarks regarding the June 17, 2011, Rule 48(b) – Request for Correction of Inventorship likewise be withdrawn from the record of the above-captioned application: (1) Second Preliminary Amendment submitted on June 17, 2011, p. 17, lns. 11-13; and (2) Amendment and Response and Petition for Extension of Time submitted on May 31, 2012, p. 25, lns. 3-7.

A petition fee of \$400.00 pursuant to 37 C.F.R. § 1.17(f) is paid concurrently herewith. Any additional fees deemed necessary may be deducted from, or any overpayments credited to, Deposit Account No. 50-3939.

Applicants' undersigned attorneys may be reached in their New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to the address given below.

Respectfully submitted,

/Alicia A. Russo/

Alicia A. Russo

Registration No.: 46,192

Erin J.D. Austin

Registration No.: 66,532

Attorneys for Applicants

FITZPATRICK, CELLA, HARPER & SCINTO
1290 Avenue of the Americas
New York, New York 10104
Facsimile: (212) 218-2200

Electronic Patent Application Fee Transmittal				
Application Number:		13099671		
Filing Date:		03-May-2011		
Title of Invention:		NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS		
First Named Inventor/Applicant Name:		Michael Joseph Sofia		
Filer:		Erin Julia Daida Austin/Wendy Valdez		
Attorney Docket Number:		03956.053800.1		
Filed as Large Entity				
Utility under 35 USC 111(a) Filing Fees				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Petition fee- 37 CFR 1.17(f) (Group I)	1462	1	400	400
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Total in USD (\$)				400

Electronic Acknowledgement Receipt	
EFS ID:	14335603
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	104538
Filer:	Erin Julia Daida Austin/DAVID NGUY
Filer Authorized By:	Erin Julia Daida Austin
Attorney Docket Number:	03956.053800.1
Receipt Date:	29-NOV-2012
Filing Date:	03-MAY-2011
Time Stamp:	13:17:46
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$ 400
RAM confirmation Number	15194
Deposit Account	503939
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees) Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Petition for review by the Office of Petitions.	039560538001_PetitiontoWithdraw48bRequest.pdf	86383 039560538001_PetitiontoWithdraw48bRequest.pdf	no	3

Warnings:**Information:**

2	Fee Worksheet (SB06)	fee-info.pdf	30463 fee-info.pdf	no	2
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Warnings:**Information:**

Total Files Size (in bytes):	116846
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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.

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(b).

I hereby appoint:



Practitioners associated with the 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 assignment documents attached to this form in accordance with 37 CFR 3.73(b).

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



The address associated with Customer Number:

117796

OR

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

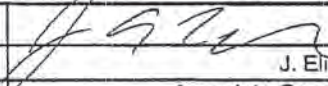
Assignee Name and Address:

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(b) (Form PTO/SB/96 or equivalent) is required to be filed in each application in which this form is used. The statement under 37 CFR 3.73(b) may be completed by one of the practitioners appointed in this form if the appointed practitioner is authorized to act on behalf of the assignee, 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.

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

STATEMENT UNDER 37 CFR 3.73(b)

Applicant/Patent Owner: Gilead Pharmasset LLC

Application No./Patent No.: 8,334,270

Filed/Issue Date: 12/18/2012

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 it is:

1. ☒ the assignee of the entire right, title, and interest in;
2. ☐ an assignee of less than the entire right, title, and interest in
(The extent (by percentage) of its ownership interest is _____ %); or
3. ☐ the assignee of an undivided interest in the entirety of (a complete assignment from one of the joint inventors was made)

the patent application/patent identified above, by virtue of either:

- 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 therefore is attached.

OR

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

1. From: Michael Joseph SOFIA, et al.

To: Pharmasset, Inc.

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

Reel 029631, Frame 0199, 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 028081, Frame 0686, or for which a copy thereof is attached.

3. From: _____

To: _____

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

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

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

- ☒ As required by 37 CFR 3.73(b)(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.

Signature

N Thakur

Date

6/23/2014

Printed or Typed Name

Neeta C. Thakur (Reg No: 59,123)

Agent for Applicant

Title

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.

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

Electronic Acknowledgement Receipt	
EFS ID:	19542006
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	104538
Filer:	Lorna Lea Tanner/Elizabeth Gutierrez
Filer Authorized By:	Lorna Lea Tanner
Attorney Docket Number:	03956.053800.1
Receipt Date:	10-JUL-2014
Filing Date:	03-MAY-2011
Time Stamp:	13:13:25
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		POA-199059-US2.PDF	298809 690d4f10e0297a315a4c0f509bdc30f50c1ed5	yes	2

Multipart Description/PDF files in .zip description			
Document Description		Start	End
Power of Attorney		1	1
Assignee showing of ownership per 37 CFR 3.73.		2	2

Warnings:

Information:

Total Files Size (in bytes):	298809
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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.



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
13/099,671	05/03/2011	Michael Joseph Sofia	03956.053800.1

104538

Fitzpatrick Cella Harper & Scinto (Gilead)
1290 Avenue of the Americas
New York, NY 10104

CONFIRMATION NO. 1344
POWER OF ATTORNEY NOTICE



Date Mailed: 07/16/2014

NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 07/10/2014.

- The Power of Attorney to you in this application has been revoked by the assignee who has intervened as provided by 37 CFR 3.71. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

/s/brahim/

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
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
13/099,671	05/03/2011	Michael Joseph Sofia	03956.053800.1

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

CONFIRMATION NO. 1344
POA ACCEPTANCE LETTER



Date Mailed: 07/16/2014

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 07/10/2014.

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.

/s/brahim/

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

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**CHANGE OF
CORRESPONDENCE ADDRESS
Patent**Address to:
Mail Stop Post Issue
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Patent Number	8,334,270
Issue Date	12-18-2012
Application Number	13/099671
Filing Date	05-03-2011
First Named Inventor	Michael Joseph SOFIA
Attorney Docket Number	37JD-199059-US2

Please change the Correspondence Address for the above-identified patent to:

☒ The address associated with Customer Number:

124963

OR

☐ Firm or
Individual Name

Address

City

State

ZIP

Country

Telephone

Email

This form cannot be used to change the data associated with a Customer Number. To change the data associated with an existing Customer Number use "Request for Customer Number Data Change" (PTO/SB/124).

This form will not affect any "fee address" provided for the above-identified patent. To change a "fee address" use the "Fee Address Indication Form" (PTO/SB/47).

I am the:

- ☐ Patentee.
- ☐ Assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).
- ☒ Attorney or agent of record. Registration Number 50782

Signature /Lorna L. Tanner/

Typed or
Printed Name Lorna L. Tanner

Date 03-31-2015

Telephone 650-815-2600

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

☐ *Total of _____ forms are submitted.

This collection of information is required by 37 CFR 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. 422 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: Mail Stop Post Issue, 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.

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.

Electronic Acknowledgement Receipt	
EFS ID:	21934458
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	117796
Filer:	Lorna Lea Tanner/Kory Mingus
Filer Authorized By:	Lorna Lea Tanner
Attorney Docket Number:	37JD-199059-US2
Receipt Date:	31-MAR-2015
Filing Date:	03-MAY-2011
Time Stamp:	18:29:08
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	Change of Address	PH3080PC2_ChangeOfCorrespondence_37JD-199059-US2.pdf	144774 1bbes62975a8f62b97dbbce0f021ae717a056475c	no	2

Warnings:

Information:

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.

PATENT - POWER OF ATTORNEY OR REVOCATION OF POWER OF ATTORNEY WITH A NEW POWER OF ATTORNEY AND CHANGE OF CORRESPONDENCE ADDRESS	Patent Number	8,334,270
	Issue Date	12-18-2012
	First Named Inventor	Michael Joseph SOFIA
	Title	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
	Attorney Docket Number	PH3080.PC2

I hereby revoke all previous powers of attorney given in the above-identified patent.

☐ A Power of Attorney is submitted herewith.

OR

☒ I hereby appoint Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s) with respect to the patent identified above, and to transact all business in the United States Patent and Trademark Office connected therewith: 124963

OR

☐ I hereby appoint Practitioner(s) named below as my/our attorney(s) or agent(s) with respect to the patent identified above, and to transact all business in the United States Patent and Trademark Office connected therewith:

Practitioner(s) Name	Registration Number

Please recognize or change the correspondence address for the above-identified patent to:

☒ The address associated with the above-mentioned Customer Number.

OR

☐ The address associated with Customer Number:

OR

☐ Firm or Individual Name

Address

City

State

Zip

Country

Telephone

Email

I am the:

☐ Inventor, having ownership of the patent.

OR

☒ Patent owner.

Statement under 37 CFR 3.73(b) (Form PTO/SB/86) submitted herewith or filed on _____

SIGNATURE of Inventor or Patent Owner

Signature	<i>Lawrence F. Rozsnyai</i>	Date	April 02, 2015
Name	Lawrence F. Rozsnyai	Telephone	415-205-9936
Title and Company	Patent Counsel, Gilead Pharmaceuticals LLC		

NOTE: Signatures of all the inventors or patent owners of the entire interest or their representatives(s) are required. Submit multiple forms if more than one signature is required, see below.

☐ Total of _____ forms are submitted.

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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Electronic Acknowledgement Receipt	
EFS ID:	21963624
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	124963
Filer:	Lawrence F. Rozsnyai/Sylvia Brennan
Filer Authorized By:	Lawrence F. Rozsnyai
Attorney Docket Number:	37JD-199059-US2
Receipt Date:	03-APR-2015
Filing Date:	03-MAY-2011
Time Stamp:	11:38:01
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		PH3080PC2_2015_04_02_State ment373_as_Filed.PDF	234510 bb002ace076767cc6d8354d6d0752b0d -1000000	yes	2

Multipart Description/PDF files in .zip description			
Document Description		Start	End
Assignee showing of ownership per 37 CFR 3.73		1	1
Power of Attorney		2	2

Warnings:

Information:

Total Files Size (in bytes):	234510
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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.

STATEMENT UNDER 37 CFR 3.73(b)

Applicant/Patent Owner: Gilead Pharmasset LLC

Application No./Patent No.: 8,334,270

Filed/Issue Date: 12-18-2012

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 it is:

1. ☒ the assignee of the entire right, title, and interest in;
2. ☐ an assignee of less than the entire right, title, and interest in
(The extent (by percentage) of its ownership interest is _____ %); or
3. ☐ the assignee of an undivided interest in the entirety of (a complete assignment from one of the joint inventors was made)

the patent application/patent identified above, by virtue of either:

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 therefore is attached.

OR

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

1. From: Michael Joseph SOFIA, et al To: Pharmasset, Inc.

The document was recorded in the United States Patent and Trademark Office at
Reel 029631, Frame 0199, 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 028081, Frame 0688, or for which a copy thereof is attached.

3. From: _____ To: _____

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

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

☒ As required by 37 CFR 3.73(b)(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.

Lawrence F. Rozsnyai
Signature

April 02, 2013
Date

Lawrence F. Rozsnyai (Reg No: 58,427)

Patent Counsel

Printed or Typed Name

Title

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.

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



UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/099,671	05/03/2011	Michael Joseph Sofia	37ID-199059-US2

124963
Gilead Pharmasset LLC
c/o Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

CONFIRMATION NO. 1344
POWER OF ATTORNEY NOTICE



Date Mailed: 04/09/2015

NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/03/2015.

- The Power of Attorney to you in this application has been revoked by the assignee who has intervened as provided by 37 CFR 3.71. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

/tkim/

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
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
13/099,671	05/03/2011	Michael Joseph Sofia	PH3080.PC2

124963
Gilead Pharmasset LLC
c/o Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

CONFIRMATION NO. 1344
POA ACCEPTANCE LETTER



Date Mailed: 04/09/2015

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/03/2015.

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.

/tkim/

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

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(b).

I hereby appoint:

☒ Practitioners associated with the 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 assignment documents attached to this form in accordance with 37 CFR 3.73(b).

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

☒ The address associated with Customer Number:

117796

OR

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

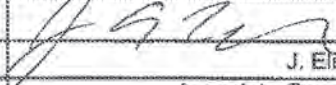
Assignee Name and Address:

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(b) (Form PTO/SB/95 or equivalent) is required to be filed in each application in which this form is used. The statement under 37 CFR 3.73(b) may be completed by one of the practitioners appointed in this form if the appointed practitioner is authorized to act on behalf of the assignee, 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.

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

STATEMENT UNDER 37 CFR 3.73(b)Applicant/Patent Owner: Gilead Pharmasset LLCApplication No./Patent No.: 8,334,270 Filed/Issue Date: December 18, 2012Titled: NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

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

states that it is:

1. ☒ the assignee of the entire right, title, and interest in;
2. ☐ an assignee of less than the entire right, title, and interest in
 (The extent (by percentage) of its ownership interest is _____ %); or
3. ☐ the assignee of an undivided interest in the entirety of (a complete assignment from one of the joint inventors was made) the patent application/patent identified above, by virtue of either:
- 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 therefore is attached.

OR

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

1. From: Michael Joseph Sofia et al. To: Pharmasset, Inc.
 The document was recorded in the United States Patent and Trademark Office at
 Reel 029631, Frame 0199, or for which a copy thereof is attached.
2. From: Pharmasset, Inc. To: Gilead Pharmasset LLC
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☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

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

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

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

/Lorna L. Tanner/
 Signature
Lorna L. Tanner (Reg. No.: 50,782)
 Printed or Typed Name

April 17, 2017
 Date
Attorney for Applicant
 Title

Corrected Application Data Sheet

Application Information

Application number::	<u>13/099,671</u>
Filing Date::	<u>05/03/11</u>
Application Type::	Continuation
Subject Matter::	Utility
Suggested Group Art Unit::	<u>1621</u>
CD-ROM or CD-R?::	None
Sequence submission?::	None
Computer Readable Form (CRF)?::	No
Title::	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
Attorney Docket Number::	~~60137-0034~~ USC1 <u>37JD-199059-US2</u>
Request for Early Publication?::	No
Request for Non-Publication?::	No
Suggested Drawing Figure::	None
Total Drawing Sheets::	0
Small Entity?::	~~Yes~~ <u>No</u>
Petition included?::	No
Secrecy Order in Parent Appl.?::	No

Applicant Information

Applicant Authority Type:: Inventor
Primary Citizenship Country:: United States
Status:: Full Capacity
Given Name:: Michael
Middle Name:: Joseph
Family Name:: Sofia
City of Residence:: Doylestown
State or Province of Residence:: PA
Country of Residence:: US
Street of mailing address:: 3066 Antler Drive
City of mailing address:: Doylestown
State or Province of mailing address:: PA
Postal or Zip Code of mailing address:: 18901

Applicant Authority Type:: Inventor
Primary Citizenship Country:: United States
Status:: Full Capacity
Given Name:: Jinfa
Family Name:: Du
City of Residence:: New Hope
State or Province of Residence:: PA
Country of Residence:: US

Street of mailing address:: 1206 Reins Circle
City of mailing address:: New Hope
State or Province of mailing address:: PA
Postal or Zip Code of mailing address:: 18938

Applicant Authority Type:: Inventor
Primary Citizenship Country:: China
Status:: Full Capacity
Given Name:: Peiyuan
Family Name:: Wang

City of Residence:: Glen Rock
State or Province of Residence:: NJ
Country of Residence:: US
Street of mailing address:: 20 Radburn Road
City of mailing address:: Glen Rock
State or Province of mailing address:: NJ
Postal or Zip Code of mailing address:: 07452

Applicant Authority Type:: Inventor
Primary Citizenship Country:: United States
Status:: Full Capacity
Given Name:: Dhanapalan
Family Name:: Nagarathnam

City of Residence:: Bethany
State or Province of Residence:: CT
Country of Residence:: US
Street of mailing address:: 52 Virginia Rail Drive
City of mailing address:: Bethany
State or Province of mailing address:: CT
Postal or Zip Code of mailing address:: 06524

Correspondence Information

Correspondence Customer Number:: ~~23552~~ 117796

Representative Information

Representative Customer Number:: ~~23552~~ 117796

Domestic Priority Information

Application::	Continuity Type::	Parent Application::	Parent Filing Date::
13/099,671	Continuation of	12/053,015	03/21/2008
12/053,015	An application claiming the benefit under 35 USC 119(e)	60/909,315	03/30/2007
12/053,015	An application claiming the benefit under 35 USC 119(e)	60/982,309	10/24/2007

Foreign Priority Information

Assignee Information

Assignee name:: Pharmasset, Inc. Gilead Pharmasset LLC

Street of mailing address:: 303 A College Road East c/o Gilead
Sciences, Inc.
333 Lakeside Drive

City of mailing address:: Princeton Foster City

State or Province of mailing address:: NJ CA

Postal or Zip Code of mailing address:: 08540 94404

Signature:

A signature of the applicant or representative is required in accordance with 37 CFR 1.33 and 10.18. Please see 37 CFR 1.4(d) for the form of the signature.			
Signature	/Lorna L. Tanner/	Date	2017-04-17
Name	Lorna L. Tanner	Registration No.	50,782

Electronic Acknowledgement Receipt	
EFS ID:	28945260
Application Number:	13099671
International Application Number:	
Confirmation Number:	1344
Title of Invention:	NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS
First Named Inventor/Applicant Name:	Michael Joseph Sofia
Customer Number:	124963
Filer:	Lorna Lea Tanner/Christa Carter
Filer Authorized By:	Lorna Lea Tanner
Attorney Docket Number:	PH3080.PC2
Receipt Date:	17-APR-2017
Filing Date:	03-MAY-2011
Time Stamp:	16:08:51
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	Power of Attorney	199059US2_POA.pdf	173857 d316ca09185a2ref0645618a3d65e25b970 1905	no	8

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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:

Total Files Size (in bytes):

173857

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New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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



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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/099,671	05/03/2011	Michael Joseph Sofia	PH3080.PC2

CONFIRMATION NO. 1344
POA ACCEPTANCE LETTER

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



Date Mailed: 04/21/2017

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/17/2017.

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

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

/vnguyen/



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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/099,671	05/03/2011	Michael Joseph Sofia	PH3080.PC2

124963
Gilead Pharmasset LLC
c/o Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

CONFIRMATION NO. 1344
POWER OF ATTORNEY NOTICE



Date Mailed: 04/21/2017

NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/17/2017.

- The Power of Attorney to you in this application has been revoked by the assignee who has intervened as provided by 37 CFR 3.71. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

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

/vnguyen/

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INITIATIVE FOR MEDICINES, ACCESS & KNOWLEDGE (I-MAK), INC.,
Petitioner,

v.

GILEAD PHARMASSET LLC,
Patent Owner.

IPR2018-00122
Patent 8,334,270 B2

Before LORA M. GREEN, GRACE KARAFFA OBERMANN, and
WESLEY B. DERRICK, *Administrative Patent Judges*.

DERRICK, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314(a)

I. INTRODUCTION

Initiative for Medicines, Access & Knowledge (I-MAK), Inc. (“Petitioner”) requests an *inter partes* review of claims 1, 2, 10–18, and 20–25 of U.S. Patent 8,334,270 B2 (Ex. 1001, “the ’270 patent”). Paper 2 (“Pet.”). Gilead Pharmasset LLC (“Patent Owner”) filed a Preliminary Response. Paper 9 (“Prelim. Resp.”).

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314(b); 37 C.F.R. § 42.4(a). We may not institute an *inter partes* review “unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a). Applying that standard, for the reasons set forth below, we decline to institute an *inter partes* review because the Petitioner has not shown a reasonable likelihood that it would prevail in establishing the unpatentability of any challenged claim.

II. BACKGROUND

A. Related Proceedings

The parties identify a concurrently filed, second petition for *inter partes* review of the ’270 patent, IPR2018-00121. Pet. 2; Paper 4, 3. Patent Owner also identifies additional petitions for *inter partes* review of additional patents: IPR2018-00119 and IPR2018-00120 for U.S. Patent No. 7,964,580 B2; IPR2018-00103 for U.S. Patent No. 7,429,572 B2; IPR2018 00125 for review of U.S. Patent No. 8,633,309 B2; and IPR2018-00126 for review of U.S. Patent No. 9,284,342 B2. Paper 4, 3.

B. The '270 Patent (Ex. 1001)

The '270 patent is directed to, *inter alia*, phosphoramidate prodrugs of a nucleoside derivative for treatment of viral infections in mammals, its ester, or a stereoisomer thereof. Ex. 1001, Abstract. The '270 patent also addresses methods of treatment, uses, and processes for preparing such compounds. *Id.* The '270 patent claims the benefit of priority of two earlier-filed provisional applications, 60/909,315, filed on March 30, 2007, and 60/982,309, filed on October 24, 2007. Ex. 1001, 1:4–9.

C. Illustrative Claims

Independent claims 1 and 16, each reciting a number of different phosphoramidate nucleoside derivatives, are reproduced below in part:

1. A compound selected from among

...

(S)-isopropyl 2-(((S)-(((2R,3R,4R, 5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyl[-] tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl) amino)propanoate

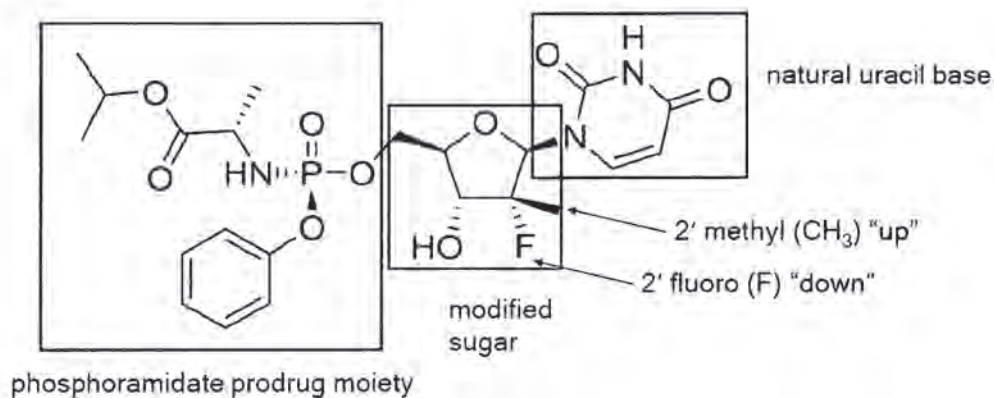
16. A compound or its stereoisomer thereof selected from among

...

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

Ex. 1001, 605:35, 52–55, 607:58–59, 608:58–61.

The compound set forth by name in the reproduced portion of claim 1 above is the Sp stereoisomer of a phosphoramidate nucleoside derivative, known as sofosbuvir, which structure is depicted below:



Prelim. Resp. 3–4. The figure depicts the chemical structure of sofosbuvir with stereochemistry and identifies the compound's phosphoramidate prodrug moiety, modified sugar, and natural uracil base. *Id.* at 4. Claim 16 likewise, in setting forth a compound or stereoisomer of compounds identified by name, including that reproduced above, encompasses the Sp stereoisomer, the Rp stereoisomer, and mixtures of the two. *Id.* at 4, 11.

D. The Asserted Grounds of Unpatentability

Petitioner asserts that claims 1, 2, 10–18, and 20–25 of the '270 patent are unpatentable based on the following grounds. Pet. 3.

References	Statutory Basis
Clark '147, ¹ Clark 2005, ² and Perrone ³	§ 103
Clark '147, Clark 2005, and McGuigan ⁴	§ 103

¹ Clark, WO 2005/003147 A2, published January 13, 2005 (Ex. 1006).

² Clark et al., 48 J. MED. CHEM. 5504–08 (2005) (Ex. 1007).

³ Perrone et al., 50 J. MED. CHEM. 1840–49 (2007) (Ex. 1008).

⁴ McGuigan, WO 2005/012327 A2, published February 10, 2005 (Ex. 1009).

Petitioner supports the Petition with the testimony of Joseph M. Fortunak, Ph.D. (Ex. 1002). Based on Dr. Fortunak's statement of qualifications (*id.* ¶¶ 1–20) and curriculum vitae (Ex. 1003), on this record, we determine that he is qualified to opine from the perspective of a person of ordinary skill in the art.

III. ANALYSIS

A. Level of Ordinary Skill in the Art

Petitioner contends that a person of ordinary skill in the art would have held either

- (1) a Ph.D. in chemistry or a closely related field with some experience in an academic or industrial laboratory focusing on drug discovery or development, and would also have some familiarity with antiviral drugs and their design and mechanism of action, or
- (2) a Bachelor's or Master's degree in chemistry or a closely related field with significant experience in an academic or industrial laboratory focusing on drug discovery and/or development for the treatment of viral diseases.

Pet. 5–6 (citing Ex. 1002 ¶ 35).

Patent Owner does not expressly contest the level of ordinary skill.
See generally Prelim. Resp.

On this record, we adopt Petitioner's essentially uncontested definition of the level of ordinary skill. We further note that the prior art itself demonstrates the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that "specific findings on the level of skill in the art . . . [are not required] 'where the prior art itself reflects an appropriate level and a need for

testimony is not shown” (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))).

B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to their broadest reasonable construction in light of the specification of the patent in which they occur. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, we interpret claim terms using “the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant’s specification.” *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997). “Under a broadest reasonable interpretation, words of the claim must be given their plain meaning, unless such meaning is inconsistent with the specification and prosecution history.” *Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1062 (Fed. Cir. 2016). If an inventor acts as his or her own lexicographer, the definition must be set forth with reasonable clarity, deliberateness, and precision. *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1249 (Fed. Cir. 1998). Only those terms which are in controversy need to be construed and only to the extent necessary to resolve the controversy. See *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017).

Petitioner contends that “there is no reason to give any of the terms of the claims of the ‘270 [patent] a meaning other than their ordinary and accustomed meaning.” Pet. 6.

Patent Owner does not contest that the claim terms should be given their ordinary and accustomed meaning. *See generally* Prelim. Resp. We determine that no claim term requires express construction for the purpose of determining whether to institute review.

C. Prior Art

1. Clark ‘147 (Ex. 1006)

Clark ‘147 teaches (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleosides, pharmaceutically acceptable salts, and prodrugs, and their use in treating hepatitis C infection. Ex. 1006, 1 (Abstract). Clark ‘147 teaches a general formula with substituents specified by reference to listings of what the substituents may be, some of which, if selected, would result in a phosphate or stabilized phosphate prodrug of (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl uridine. Ex. 1006, 18:3–20:11, 47:16–25. Clark ‘147 also discloses that (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl cytidine has anti-viral activity, including against HCV (*id.* at 88:16–89:30) and lower toxicity than certain other nucleoside analogs (*id.* at 90:1–27).

2. Clark 2005 (Ex. 1007)

Clark 2005 reports the synthesis of the (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl analogs of both cytidine and uridine, these analogs' level of anti-HCV activity, and their level of cytotoxicity. Ex. 1007, 1, 3. Clark 2005 reports that the cytidine analog, i.e., compound 1, has anti-HCV activity and low cellular toxicity. *Id.* Clark 2005 reports that the uridine analog, i.e.,

compound 9, “demonstrated no activity or cytotoxicity in any assay.” *Id.* at 3.

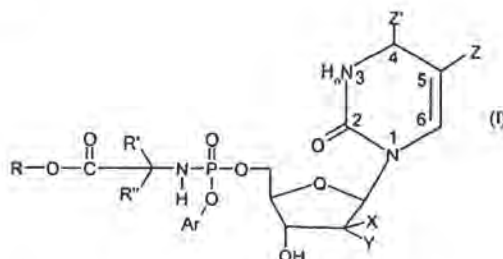
3. *Perrone (Ex. 1008)*

Perrone reports that “4’-[a]zidouridine did not inhibit HCV, although 4’-azidocytidine was a potent inhibitor of HCV replication under similar assay conditions” and that “4’-azidouridine triphosphate was a potent inhibitor of RNA synthesis by HCV polymerase.” Ex. 1008, 1. Perrone reports the synthesis of a number of different phosphoramidate derivatives of 4’-azidouridine, their level of anti-HCV activity, and their level of cytotoxicity. *Id.* at 2–4. The derivatives include phenyl phosphoramidate and 1-naphthyl nucleotide derivatives,⁵ including one derivative, compound 15, with a phenyl L-alanine isopropyl ester phosphoramidate moiety. *Id.* at 4. Perrone further teaches that the reported results “demonstrate[] the ability . . . to successfully bypass the rate limiting initial phosphorylation of a ribonucleoside analogue and thus confer significant antiviral activity on an inactive parent nucleoside.” *Id.* at 5.

4. *McGuigan (Ex. 1009)*

McGuigan teaches nucleotide derivatives according to a general formula I, reproduced below, with substituents Ar, Q, R, R’, R’’, X, Y, Z, and Z.

⁵ Perrone states that “the phenyl substituent on the phosphate [of the phenyl phosphoramidate was replaced] with . . . 1-naphthyl” in the 1-naphthyl analogs. Ex. 1008, 4; *see also id.* (Scheme 3, Tables 1 & 3), *id.* at 4 (Fig. 2).



Ex. 1009, 5:11–14. Formula I depicts common structure and points of substitution with substituents. *Id.* McGuigan sets forth different possibilities for these substituents. *Id.* at 5:16–6:8, 7:22–13:22.

D. Alleged Unpatentability of the Challenged Claims

1. Obviousness over Clark '147, Clark 2005, and Perrone

Petitioner contends that claims 1, 2, 10–18, and 20–25 are unpatentable as obvious over the combination of Clark '147, Clark 2005, and Perrone. Pet. 28–44.

Claims 1 and 2 each “recite [a] Markush Group[] of compounds that include[s], ‘(S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate,’” and claims 16–18 “recite [a] Markush [Group] of compounds that include, ‘(S)-2-[[[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-yl)methoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester.’” *Id.* at 28 (citing Ex. 1001, 605:35–606:63, 607:57–616:23). The Petitioner identifies these compounds as “5’-phosphate (phosphoramidate) prodrugs of the uridine analog ‘(2’R)-2’-deoxy-2’-fluoro-2’-C-methyluridine’, wherein the 5’-

phosphate group is the ‘(phenyl)(isopropyl-L-alaninyl)phosphate’ group.” *Id.* at 28–29 (citing Ex. 1001, 493:42–46; Ex. 1002 ¶ 160).

Petitioner sets forth its obviousness ground on the basis of one specific uridine analog—2'-deoxy-2'-fluoro-2'-C-methyluridine—with one specific phosphoramidate moiety—(phenyl)(isopropyl-L-alaninyl)phosphate. *See, e.g.*, Pet. 36 (“claims 1, 2, and 16-18 are different from Clark ‘147 only in that the stable 5'-phosphate group on the nucleoside analog . . . is the ‘(phenyl)(isopropyl-L-alaninyl)phosphate’ group”); *id.* at 39 (“Applying Perrone’s ProTide approach to Clark ‘147 and Clark 2005’s promising nucleoside would result in *the compound* claimed in claims 1, 2, and 16-18 More specifically, Perrone taught that a stable modified 5'-phosphate group . . . is the ‘(phenyl)(isopropyl-L-alaninyl)phosphate’ group” (emphasis added)); *id.* at 41–42 (relying on Perrone’s teaching as to the “use of the ‘(phenyl)(isopropyl-L-alaninyl)phosphate’ group”). In limiting its analysis in that way, Petitioner fails to set forth how, or if, any other compound recited in the Markush groups of claims 1, 2, and 16–18, would be rendered obvious by the cited references. *See generally* Pet.

Petitioner relies generally on Clark '147 and Clark 2005 for the 2'-deoxy-2'-fluoro-2'-C-methyluridine nucleoside and on Perrone for the phosphoramidate moiety. Petitioner contends that one of ordinary skill in the art, informed by the teachings of Clark '147 and Clark 2005, would have been led to 2'-deoxy-2'-fluoro-2'-C-methyluridine, a known nucleoside compound, and motivated “to use the well-known strategy to select a suitable stable 5'-phosphate group for (2'R)-2'-deoxy-2'-fluoro-2'-C-methyluridine . . . in order to increase its activity.” *Id.* at 28–37. As to the “suitable stable 5'-phosphate group” (*id.* at 37), Petitioner contends that

“[o]ne would have been specifically motivated to refer to Perrone, which taught a phosphoramidate ‘ProTide’ approach to confer potency against hepatitis C virus by activating otherwise inactive nucleosides” (*id.* at 37–38).

Petitioner maintains Clark ’147 suggests or teaches the nucleoside analog. Petitioner relies on Example 5 of Clark ’147, which discloses that (2’R)-2’-deoxy-2’-fluoro-2’-C-methyl-cytidine has anti-viral activity, including against HCV (Ex. 1006, 88:16–89:30), and lower toxicity than certain other nucleoside analogs (*id.* at 90:1–27). Petitioner further relies on the common knowledge that uracil is one of the four bases in RNA, and contends that “a [person of ordinary skill in the art] would have been motivated to replace the cytidine in the active (2’R)-2’-deoxy-2’-fluoro-2’-C-methylcytidine 5’-triphosphate with a uridine,” and also that they would have “had an expectation that this would produce a likewise active and potent HCV inhibitor.” Pet. 33–34 (citing Ex. 1002 ¶ 168).

Petitioner maintains Clark ’147 also suggests or teaches phosphorylated, or prodrug forms, of the nucleoside analog. Petitioner contends that “a [person of ordinary skill in the art] would have been . . . fully motivated to specifically choose, from the various compounds encompassed by Claim 40 [of Clark ’147], the 5’-phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug) of (2’R)-2’-deoxy-2’-fluoro-2’-C-methyl uridine as a practicable HCV inhibitor.” Pet. 34 (citing Ex. 1002 ¶ 169). Petitioner further relies on a portion of Clark ’147 that reads:

A number of nucleotide prodrug ligands are known. In general, alkylation, acylation or other lipophilic modification of the mono-, di- or triphosphate of the nucleoside reduces polarity and allows passage into cells. . . . Any of these can be used in

combination with the disclosed nucleosides to achieve a desired effect.

Pet. 35–36 (quoting Ex. 1006, 58:15–24, with added emphasis); Ex. 1002 ¶ 172. Petitioner contends Clark '147 “explicitly [teaches] that alkylation, acylation, arylation, or other lipophilic modification can be made to the phosphate group in the 5'-phosphate of (2'R)-2'-deoxy-2'-C-methyluridine to increase its activity, bioavailability and stability, and that the modified prodrug will convert into the 5'-monophosphate form (U'MP) after its entry into the cell.” Pet. 36 (citing Ex. 1002 ¶ 173).

Clark 2005 discloses the nucleoside analog. Petitioner relies on Clark 2005's report that the (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl analog of cytidine—compound 1—has anti-HCV activity and low cytotoxicity and that the uridine analog—compound 9—has “no activity or cytotoxicity in any assay.” *Id.* at 36–37; Ex. 1007, 1, 3. Petitioner also relies on Clark 2005, without elaboration, as teaching “that the cytidine form of the Clark '147 nucleoside could metabolically convert *in vivo* to the uridine form.” Pet. 36 (citing Ex. 1007, 3).

Petitioner contends that “[t]he Clark 2005 results would have motivated a [person of ordinary skill in the art] to understand the lack of activity of the uridine form and to pursue methods to activate the uridine if the lack of activity were due to inefficient phosphorylation.” *Id.* at 37 (citing Ex. 1002 ¶ 178).

Petitioner also contends that “[a person of ordinary skill in the art] would investigate the 2'-deoxy-2'-fluoro-2'-C-methyluridine nucleoside in Clark 2005 as a lead compound.” Pet. 41 (citing Ex. 1002 ¶ 189). In contending this, without explanation, Petitioner fails to specifically address its earlier contention, as to Clark '147, that “a [person of ordinary skill in the

art] would have been . . . fully motivated to specifically choose, from . . . the 5'-phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug) of (2'R)-2'-deoxy-2'-fluoro-2'-C-methyluridine as a practicable HCV inhibitor." Pet. 34 (citing Ex. 1002 ¶ 169). Rather, Petitioner simply settles, in effect, on the 2'-deoxy-2'-fluoro-2'-C-methyluridine nucleoside as its lead compound without adequate explanation, which suggests Petitioner relies on an improper hindsight reconstruction. Pet. 37, 41; *see* Prelim. Resp. 2 (persuasively arguing that Petitioner "provides no evidence to establish that the genus resulting from its proposed Clark '147/Clark 2005 combination is an appropriate starting point or that it is sufficiently narrow to define a lead compound").

As to the prodrug moiety, despite the teaching in Clark '147, identified above, that "[a] number of nucleotide prodrug ligands are known" and that "[a]ny of these can be used" (Pet. 35–36 (quoting Ex. 1006, 58:17, 23–24); Ex. 1002 ¶ 172), Petitioner contends that "[o]ne would have been specifically motivated to refer to Perrone [Ex. 1008], which taught a phosphoramidate 'ProTide' approach to confer potency against hepatitis C virus by activating otherwise inactive nucleosides" (Pet. 37–38). Petitioner's declarant identifies increased activity and reduced toxicity as improvements desired in modifying a lead compound. Ex. 1002 ¶ 32. Petitioner also contends, in respect to compositions, that "Perrone also taught that applying its phosphoramidate ProTide approach to nucleosides could activate them as HCV inhibitors for use in treating people." Pet. 43 (citing Ex. 1008, 1); Ex. 1002 ¶ 199.

Petitioner further contends that a person of ordinary skill in the art would have "had a reasonable expectation of success . . . because of the

general knowledge that nucleosides needed to be phosphorylated to [be] active in HCV replication and the fact that Perrone provided several examples of comparable nucleosides being triphosphorylated by its ProTide approach.” Pet. 38–39; Ex. 1002 ¶ 182. Petitioner maintains that “[i]n considering the similarity of Clark ‘147, Clark 2005 and Perrone, a [person of ordinary skill in the art] would not focus on the structural differences between the parent nucleosides, 2'-deoxy-2'-fluoro-2'-C-methyluridine and 4'-aziduridine [sic, 4'-azidouridine].” Pet. 41; Ex. 1002 ¶ 189.

Petitioner refers to additional references, including Wagner (Ex. 1010), McGuigan 2006 (Ex. 1012), McGuigan 1994 (Ex. 1013), and Cahard (Ex. 1014), in discussing the background knowledge in the art (Pet. 15–21), and contends that “it was generally known that, for antiviral 5'-phosphate prodrugs, the antiviral activity lies in the nucleoside itself” (*id.* at 17 (citing Ex. 1002 ¶ 63)). Cahard is cited, in particular, for teaching “that the phenyl alanyl phosphoramidate approach was successful on a range of nucleosides by many research groups.” *Id.* at 15–16 (citing Ex. 1002 ¶ 56; Ex. 1014, 1, 4).

Petitioner also contends that “the range of realistic options is reasonably limited” for substitutions to (or the identity of) the amino acid moiety, the ester on the amino group, the ester group on the phosphorus, and optional substitution on nitrogen of the amino acid. Pet. 18; Ex. 1002 ¶¶ 65–66. Petitioner cites to Perrone, without further analysis, as demonstrating “how the amino acid moiety is most often glycine, alanine or valine, and how the ester group on the amino acid is most often methyl, isopropyl, or benzyl,” and contends, without cited support, that “[t]he useful ester groups

on phosphorous are aryl (typically phenyl).” Pet. 18; Ex. 1002 ¶¶ 65–66; Ex. 1008.

Although Petitioner cites to Wagner (Ex. 1010), McGuigan 2006 (Ex. 1012), McGuigan 1994 (Ex. 1013), and Cahard (Ex. 1014), including in referring to specific compounds, Petitioner provides little, if any, analysis as to the effects of the various disclosed substitutions (or identities) of various elements of the phosphoramidate moiety (*see, e.g.*, Pet. 17, 42 (citing Ex. 1012, 1, 4), 14–15, 17 (citing Ex. 1013, 3), 16–17 (citing Ex. 1014, 2–3)). Petitioner also does not provide particular analysis or evidence to support its implicit contention that the effect of any particular phosphoramidate, or other prodrug, moiety of a nucleoside analog prodrug is independent of the structure of the parent nucleoside analog. *See generally* Pet.

As to Perrone’s disclosure, Petitioner emphasizes that “Perrone . . . prepared about 20 stable phosphate-based prodrugs of [4’-azidouridine]” (*id.* at 38), including compound 15 which has a phenyl L-alanine isopropyl ester phosphoramidate moiety (*id.* at 39). Petitioner maintains that “only 6 highly active phosphoramidate groups [are] particularly identified in Perrone (*i.e.* No.14, 15, 17, and 33–35)” and contends that “[a person of ordinary skill in the art] would have been motivated to try to attach each to the 5’-position of . . . (2’R)-2’-deoxy-2’-fluoro-2’-C-methyluridine resulting in the compounds of claims 1, 2, [and] 16–18.” *Id.* at 40 (citing Ex. 1002 ¶ 186; Ex. 1008, 4). Petitioner further contends that a person of ordinary skill in the art “would in particular prepare the derivatives . . . that correspond to compounds 14, 15 and 17 in Perrone because they are described as having ‘exceptional’ antiviral activity.” *Id.* at 41; Ex. 1002 ¶ 188; Ex. 1008, 3–4. As noted

above, however, the only analysis, or even mention of compounds recited in the claims, is limited to the two that Petitioner identifies as corresponding to the 5'-phosphate (phosphoramidate) prodrugs of (2R)-2-deoxy-2-fluoro-2-C-methyluridine, wherein the 5-phosphate group is the (phenyl)(isopropyl-L-alaninyl)phosphate group, the phosphoramidate moiety of Perrone's compound 15. *See generally* Pet.

Petitioner has, in effect, set forth two different, intertwined, theories of obviousness; a lead compound theory grounded on selection of 2'-deoxy-2'-fluoro-2'-C-methyluridine as a lead compound, followed by its modification, and a theory grounded on combining 2'-deoxy-2'-fluoro-2'-C-methyluridine, or the corresponding portion of a 5'-phosphate or stabilized prodrug, with the phosphoramidate moiety of a phosphoramidate 4'-azidouridine analog to arrive at claimed subject matter, in particular, the 5'-phosphate (phosphoramidate) prodrugs of (2R)-2-deoxy-2-fluoro-2-C-methyluridine, wherein the 5-phosphate group is the (phenyl)(isopropyl-L-alaninyl)phosphate group.

The lead compound analysis follows a two-part inquiry. In the first part, we “determine[] whether a chemist of ordinary skill would have selected the asserted prior art compounds as lead compounds, or starting points, for further development efforts.” *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1291 (Fed. Cir. 2012). The question of whether a person of ordinary skill in the art would have selected a compound as a lead compound is “guided by evidence of the compound’s pertinent properties.” *Id.* at 1292. In the second part, we determine whether the artisan would have had reason to modify the lead compound to make the claimed compound, and whether they “would have had a reasonable expectation of success in doing so.” *Id.*

As to the non-lead compound analysis, we simply determine whether “a skilled artisan would have had reason to combine the teaching of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success from doing so.” *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1069 (Fed. Cir. 2012) (internal quotation marks and citation omitted). “Where a skilled artisan merely pursues ‘known options’ from ‘a finite number of identified, predictable solutions,’ the resulting invention is obvious under section 103.” *Id.* at 1070 (quoting *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007)).

Evidence of obviousness, especially when that evidence is proffered in support of an “obvious-to-try” theory, is insufficient unless it indicates that the possible options skilled artisans would have encountered were “finite,” “small,” or “easily traversed,” and that skilled artisans would have had a reason to select the route that produced the claimed invention. *Id.* at 1072 (citing *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008)).

Although Patent Owner presents its arguments generally as addressing deficiencies as to a lead compound theory of obviousness (Prelim. Resp. 12–16), some arguments are applicable to both theories (*id.* at 16–29).

Patent Owner argues that Petitioner has failed to establish the requisite motivation to combine the 2'-deoxy-2'-fluoro-2'-C-methyluridine nucleoside with any of Perrone's phosphoramidate moieties, and particularly (phenyl)(isopropyl-L-alaninyl)phosphate. Prelim. Resp. 26–29. Patent Owner further argues that Petitioner ignores structural differences between 2'-deoxy-2'-fluoro-2'-C-methyluridine and Perrone's 4'-azidocytidine nucleoside and that such differences “can have a huge impact on the

properties of the final molecule, including whether the molecule is effective against HCV and whether it has toxic side effects.” *Id.* at 27–28. Patent Owner further argues that Petitioner “offers no evidence . . . that a person of ordinary skill would disregard these structural differences.” *Id.* at 28 (citing Pet. 37–41; Ex. 1002 ¶¶ 182, 189).

Patent Owner contends that “for a different nucleoside compound one would need to conduct research to determine which phosphoramidate prodrugs may or may not work.” *Id.* at 28–29. Patent Owner cites to Perrone itself as teaching that “the disclosed phosphoramidate prodrugs would be expected to behave differently if used with different parent compounds” in having “noted that ‘quite distinct [structure-activity relationships]’ were found for the particular nucleoside studied compared to nucleosides previously studied.” Prelim. Resp. 28 (citing Ex. 1008, 4).

Perrone also reports, in discussing certain phosphoramidate variants:

These results [with 4'-azidouridine] were striking when compared to the 60–70 fold reduction in anti-HIV potency for d4T ProTides with an L-alanine to glycine replacement and a 20–40 fold reduction for the corresponding abacavir ProTides. This reinforces our earlier conclusion that *a separate ProTide motif optimization process is needed for each nucleoside analogue* versus a given target.

Ex. 1008, 4 (emphasis added) (endnotes omitted).

Patent Owner similarly contends that “[a] person of ordinary skill . . . would not have had a reasonable expectation that combining Perrone’s phosphoramidate with 2'-deoxy-2'-fluoro-2'-C-methyluridine would yield an effective anti-HCV drug.” Prelim. Resp. 29. Patent Owner, in discussing the search for “effective treatments for HCV” (*id.* at 4–10), highlights that both activity and toxicity are factors (*id.* at 6) and that “changes to the

structure of a nucleoside, or a prodrug used with a nucleoside, could have unpredictable and often negative impacts on the activity and toxicity of that nucleoside” (*id.*).

We have considered Petitioner’s arguments and evidence along with the Preliminary Response, and, on this record, for reasons that follow, we agree with Patent Owner that Petitioner has not met the threshold for instituting an *inter partes* review of the ’270 patent.

We turn first to the lead compound analysis. As set forth above, Petitioner contends that Clark ’147 “explicitly taught that alkylation, acylation, arylation, or other lipophilic modification can be made to the phosphate group in the 5’-phosphate of (2’R)-2’-deoxy-2’-fluoro-2’-C-methyluridine” for improved properties and that “the 5’-phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug) . . . [are] practicable HCV inhibitor[s]” providing increased activity, bioavailability, and stability. Pet. 34, 36; Ex. 1002 ¶¶ 169, 173.

In selecting the 2’-deoxy-2’-fluoro-2’-C-methyluridine nucleoside as the lead compound, Petitioner fails to adequately explain why this particular compound was chosen over other compounds, particularly the monophosphate, or any of a number of stabilized monophosphate prodrugs. *See generally* Pet.

Also, as set forth above, Petitioner and its declarant contend that one of ordinary skill in the art with the known nucleoside 2’-deoxy-2’-fluoro-2’-C-methyluridine in hand—would turn first to Perrone for its teaching of phosphoramidate prodrug moieties, and then to those moieties that provide greater activity, without significant toxicity, in phosphoramidate

4'-azidouridines. The difficulty, however, is that Petitioner fails to set forth a sufficient showing that a person of ordinary skill in the art would have had a reasonable expectation of the same benefit with 2'-deoxy-2'-fluoro-2'-C-methyluridine.

Petitioner relies variously on asserted similarity in structure of the parent nucleosides without directly addressing the structural differences (Pet. 41; Ex. 1002 ¶ 189) and on the notion that the antiviral activity lies on the nucleoside itself (Pet. 17). This reliance is insufficient, however, in light of potentially significant differential effects on activity (and toxicity) when a particular phosphoramidate moiety is used to modify different nucleoside analogs, as highlighted by Patent Owner. *See, e.g.*, Prelim. Resp. 28–29.

Petitioner's citation to other references that disclose phosphoramidate nucleoside analog prodrugs, likewise, as discussed above, is inadequate to support trial institution because there is insufficient analysis by Petitioner, particularly as to the likelihood of obtaining useful activity without significant toxicity. *See, e.g.*, Pet. 9–17, 19–21, and 42. That is to say, in the face of evidence that the effect of a particular phosphoramidate moiety of a nucleoside analog prodrug is not independent of the structure of the parent nucleoside analog, more is required of Petitioner than general assertions that the nucleoside analogs are similar, and that similar approaches with other nucleoside analogs provided success.

Under a non-lead compound analysis, Petitioner has likewise failed to set forth a sufficient basis for obviousness, within the meaning of 35 U.S.C. § 103, to meet its threshold burden. “[O]bviousness concerns whether a skilled artisan not only *could have made* but *would have been motivated to make* the combinations or modifications of prior art to arrive at the claimed

invention.” *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015). The deficiency as to a reasonable expectation of success in obtaining an active and nontoxic agent, discussed above, is also relevant here because it goes to whether there are “identified, predictable solutions” that the skilled artisan would have been motivated to pursue at the time of the invention. *Cf. Cyclobenzaprine Hydrochloride*, 676 F.3d at 1070.

Further, Petitioner provides no sound basis for “the possible options skilled artisans would have encountered [being] ‘finite,’ ‘small,’ or ‘easily traversed.’” *Id.* at 1072 (citing *Ortho-McNeil Pharm.*, 520 F.3d at 1364). Although Petitioner contends the skilled artisan would have selected from the subset of phosphoramidate moieties associated with high activity and low toxicity when used with 4'-azidouridine disclosed in Perrone (Pet. 40–41), there is no showing by Petitioner that these options would have been the only ones expected to provide high activity and low toxicity (*see generally id.*). Likewise, there is insufficient explanation and support for the range of possible phosphoramidate being finite, small, or easily traversed.

Dr. Fortunak’s declaration essentially parrots the Petition without directing us to adequate objective proof for the bare assertions made therein, and, therefore, does not remedy the various deficiencies in Petitioner’s ground of unpatentability. *See Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 294 (Fed. Cir. 1985) (“Lack of factual support for expert opinion going to factual determinations” is sufficient to “render the testimony of little probative value in a validity determination.”).

Petitioner thus fails to bear the burden required to support institution of review. *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (“In an [*inter partes* review], the petitioner has the burden from the

onset to show with particularity why the patent it challenges is unpatentable.”). Petitioner should not expect the Board to search the record to piece together what may support a challenge. *See* 37 C.F.R. § 42.22(a)(2) (a petition must include “[a] full statement of the reasons for the relief requested”); *DeSilva v. DiLeonardi*, 181 F.3d 865, 866–67 (7th Cir. 1999) (“A brief must make all arguments accessible to the judges, rather than ask them to play archaeologist with the record.”); *cf. Magnum Oil Tools Int’l Ltd.*, 829 F.3d 1364, 1380–81 (Fed. Cir. 2016) (rejecting an argument that the Board properly “ma[de] an obviousness argument on behalf of [petitioner]” that “could have been included in a properly drafted petition,” because “petitioner . . . bears the burden of proof”).

Accordingly, we are not persuaded that Petitioner establishes a reasonable likelihood of prevailing in showing that the subject matter of any challenged claim is unpatentable over the combination of Clark ’147, Clark 2005, and Perrone.

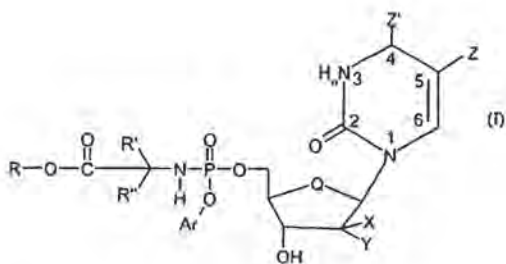
2. Obviousness over Clark ’147, Clark 2005, and McGuigan

Petitioner contends that claims 1, 2, 10–18, and 20–25 are unpatentable as obvious over the combination of Clark ’147, Clark 2005, and McGuigan. Pet. 45–58.

Petitioner contends, in the same manner as for the first ground, that one of ordinary skill in the art, informed by the teachings of Clark ’147 and Clark 2005, would have been led to 2'-deoxy-2'-fluoro-2'-C-methyluridine and motivated “to use the well-known strategy to select a suitable stable 5'-phosphate group for (2'R)-2'-deoxy-2'-fluoro-2'-C-methyluridine . . . in order to increase its activity.” *Compare* Pet. 45–54, with *id.* at 28–37.

The second ground also rests on the contention, as did the first, that the relied on prior art would have led the skilled artisan to “5’-phosphate (phosphoramidate) prodrugs of the uridine analog ‘(2’R)-2’-deoxy-2’-fluoro-2’-C-methyluridine’, wherein the 5’-phosphate group is the ‘(phenyl)(isopropyl-L-alaninyl)phosphate’ group.” Compare *id.* at 45–46, with *id.* at 28–29; see, e.g., *id.* at 53 (“claims 1, 2, and 16–18 are different from Clark ‘147 only in that the stable 5’-phosphate group on the nucleoside analog . . . is the ‘(phenyl)(isopropyl-L-alaninyl)phosphate’ group”); *id.* at 55–57 (setting forth the necessary selections from McGuigan’s disclosure to arrive at the (phenyl)(isopropyl-L-alaninyl)phosphate and concluding that “it would have been obvious . . . to obtain *the compound* of claims 1, 2 and 16–18” (emphasis added)).

Petitioner further contends that “[o]ne would have been specifically motivated to refer to” McGuigan’s formula I—reproduced below—and then to select particular substituents from the listed, possible substituents. *Id.* at 55–57.



Ex. 1009, 5:11–14. Formula I depicts common structure and points of substitution with substituents. *Id.* McGuigan sets forth different possibilities for these substituents. *Id.* at 5:16–6:8, 7:22–13:22. Petitioner emphasizes, by underlining, the selection of methyl and F from “the group

comprising H, F, Cl, Br, I, OH, and methyl (-CH₃)” for X and Y and that “Z’ is =O” rather than -NH₂. Pet. 55–56; Ex. 1002 ¶ 223.

As to the necessary selections to arrive at the phosphoramidate moiety, referring to quoted sections of McGuigan as to what is preferred, Petitioner argues that “a [person of ordinary skill in the art] would have been encouraged by McGuigan . . . to select Q=O, n=1, Z’=O, Z=H, X=CH₃, Y=F, Ar=phenyl, R=isopropyl, R’=H, and R’’=CH₃” such that “the compound of formula (I) of McGuigan . . . would be identical to the compound of claims 1, 2, 16–18.”⁶ *Id.* at 56 (citing Ex. 1002 ¶ 225). The Petition and relied on declaration both set forth that McGuigan “highlight[s] that, [p]referably, R is methyl, ethyl, *n*- or *i*-propyl” (citing McGuigan 9:20) and, as to Ar, that “[m]ore preferably, Ar is selected from the group comprising: Ph-” (citing McGuigan 13:1–2). Pet. 56; Ex. 1002 ¶ 224.

Petitioner further contends that “[a person of ordinary skill in the art] would have been motivated to select these substituents because they were indicated by McGuigan . . . to be preferred and Clark ‘147 and Clark 2005 taught the same exact sugar ring and base structure.” Pet. 56 (citing Ex. 1002 ¶ 225).

Petitioner contends that “[t]hus, it would have been obvious to a person skilled in the art to obtain the compound of claims 1, 2 and 16–18 based on Clark ‘147, Clark 2005 and McGuigan . . . in combination with the general knowledge in the art at the time.” *Id.* at 56–57 (citing Ex. 1002 ¶ 226).

⁶ In McGuigan’s formula (I), these selections, with those above as to the nucleoside, would set forth the 5’-phosphate (phosphoramidate) prodrugs of the uridine analog 2’-deoxy-2’-fluoro-2’-C-methyluridine, wherein the 5’-phosphate group is the (phenyl)(isopropyl-L-alaninyl)phosphate group.

As Patent Owner points out, however, Petitioner omits substituents that McGuigan lists in the groups as similarly preferred, and ignores substituents identified as more preferred. *Compare* Prelim. Resp. 34–35, *with* Pet. 56. As to substituent R, the relied on group is not limited to “methyl, ethyl, *n*- or *i*-propyl” (Pet. 56 (emphasis omitted)), but also includes “*n*- or *i*-butyl (-C₄H₉) or benzyl (-CH₂CH₂CH₂CH₃)” (Ex. 1009, 9:20–21). Further, McGuigan states in “[t]he next sentence . . . that ‘[m]ost preferably, **R is benzyl.**’” Prelim. Resp. 34 (quoting Ex. 1009, 9:21, with added emphasis). As to substituent Ar, similarly, the relied on group is not limited to a Ph-, but also includes “*p*CF₃CH₂CH₂CH₂CH₂-, *p*NO₂C₆H₄-, *p*ClC₆H₄- and *o*ClC₆H₄-.” Ex. 1009, 13:1–2; *see also* Prelim. Resp. 34–35. Petitioner and Dr. Fortunak thus err in setting forth what McGuigan identifies as preferred from which one of ordinary skill in the art would select substituents. On this record, Petitioner’s selection of the requisite compounds suggests an impermissible hindsight reconstruction.

Also, as highlighted by Patent Owner’s arguments contrasting the intended use of McGuigan’s phosphoramidate derivatives (Prelim. Resp. 30–31), Petitioner fails to provide a rationale why a person of ordinary skill would look to McGuigan for its teachings, but only asserts that “[o]ne would have been specifically motivated to refer to [McGuigan’s] teaching of compounds of formula (I)” (Pet. 55; Ex. 1002 ¶ 223). Petitioner directs us to no persuasive evidence nor explanation why McGuigan’s formula (I), which is described as “particularly applicable for the treatment of a patient having breast cancer, colon cancer or prostate cancer” (Ex. 1009, 17:1–2), “would be useful to treat HCV, which is a disease of the liver” (Prelim. Resp. 31).

Petitioner's failure to identify evidence sufficient to support the contention that one of ordinary skill in the art would have been motivated to select the particular substituents required to arrive at the claimed subject matter, including even the particular compound relied on in Petitioner's contention of obviousness, and is dispositive. Here again, Dr. Fortunak's declaration essentially parrots the Petition without directing us to adequate objective proof for the bare assertions made therein, and, therefore, does not remedy this deficiency. *See Ashland Oil*, 776 F.2d at 294. Lacking any sound basis for why one of ordinary skill would select the particular substituents, this ground of obviousness lacks the requisite "rational underpinning [required] to support the legal conclusion of obviousness." *KSR*, 550 U.S. at 418 (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). Petitioner thus fails to bear the burden required to support institution of review. *Harmonic*, 815 F.3d at 1363.

Accordingly, we are not persuaded that Petitioner establishes a reasonable likelihood of prevailing in showing that the subject matter of any challenged claim is unpatentable over Clark '147, Clark 2005, and McGuigan.

IV. CONCLUSION

Petitioner has not established a reasonable likelihood of prevailing on its assertion that claims 1, 2, 10–18, and 20–25 are unpatentable.

IPR2018-00122
Patent 8,334,270 B2

V. ORDER

For the reasons given, it is:

ORDERED that the Petition is *denied* as to all challenged claims of the '270 patent and no trial is instituted.

IPR2018-00122
Patent 8,334,270 B2

PETITIONER:

Daniel B. Ravicher
Ravicher Law Firm PLLC
dan@ravicher.com

PATENT OWNER:

Dorothy P. Whelan
Michael J. Kane
W. Chad Shear
FISH & RICHARDSON P.C.
whelan@fr.com
kane@fr.com
shear@fr.com

David L. Cavanaugh
Emily R. Whelan
WILMER HALE
david.cavanaugh@wilmerhale.com
emily.whelan@wilmerhale.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INITIATIVE FOR MEDICINES, ACCESS & KNOWLEDGE (I-MAK), INC.,
Petitioner,

v.

GILEAD PHARMASSET LLC,
Patent Owner.

IPR2018-00121
Patent 8,334,270 B2

Before LORA M. GREEN, GRACE KARAFFA OBERMANN, and
WESLEY B. DERRICK, *Administrative Patent Judges*.

DERRICK, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314(a)

I. INTRODUCTION

Initiative for Medicines, Access & Knowledge (I-MAK), Inc. (“Petitioner”) requests an *inter partes* review of claims 1, 2, 10–18, and 20–25 of U.S. Patent 8,334,270 B2 (Ex. 1001, “the ’270 patent”). Paper 2 (“Pet.”). Gilead Pharmasset LLC (“Patent Owner”) filed a Preliminary Response. Paper 9 (“Prelim. Resp.”).

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314(b); 37 C.F.R. § 42.4(a). We may not institute an *inter partes* review “unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a). Applying that standard, for the reasons set forth below, we decline to institute an *inter partes* review because the Petitioner has not shown a reasonable likelihood that it would prevail in establishing the unpatentability of any challenged claim.

II. BACKGROUND

A. Related Proceedings

The parties identify a concurrently-filed, second petition for *inter partes* review of the ’270 patent, IPR2018-00122. Pet., 2; Paper 4, 3. Patent Owner also identifies additional petitions for *inter partes* review of additional patents: IPR2018-00119 and IPR2018-00120 for U.S. Patent No. 7,964,580 B2; IPR2018-00103 for U.S. Patent No. 7,429,572 B2; IPR2018-00125 for review of U.S. Patent No. 8,633,309 B2; and IPR2018-00126 for review of U.S. Patent No. 9,284,342 B2. Paper 4, 3.

B. The '270 Patent (Ex. 1001)

The '270 patent is directed to, *inter alia*, phosphoramidate prodrugs of a nucleoside derivative for treatment of viral infections in mammals, its ester, or a stereoisomer thereof. Ex. 1001, Abstract. The '270 patent also addresses methods of treatment, uses, and processes for preparing such compounds. *Id.* The '270 patent claims the benefit of priority of two earlier-filed provisional applications, 60/909,315, filed on March 30, 2007 (Ex. 2013), and 60/982,309, filed on October 24, 2007 (Ex. 2014), respectively, "the '315 application" and "the '309 application." Ex. 1001, 1:4–9.

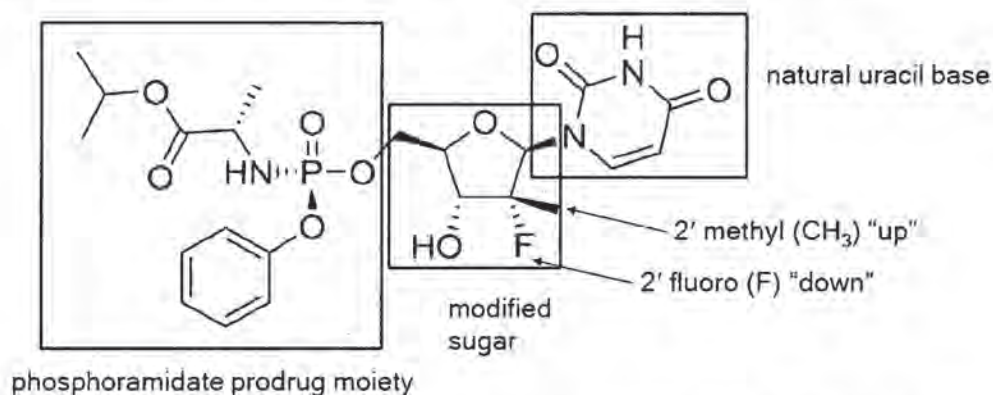
C. Illustrative Claims

Independent claims 1 and 16, each reciting a number of different phosphoramidate nucleoside derivatives, are reproduced below in part:

1. A compound selected from among
...
(S)-isopropyl 2-(((S)-(2R,3R,4R, 5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyl[-]tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate
16. A compound or its stereoisomer thereof selected from among
...
(S)-2-{{{(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydrofuran-2-ylmethoxy}-phenoxy-phosphorylamino}-propionic acid isopropyl ester

Ex. 1001, 605:35, 52–55, 607:58–59, 608:58–61.

The compound set forth by name in the reproduced portion of claim 1 above is the *Sp* stereoisomer of a phosphoramidate nucleoside derivative, known as sofosbuvir, which structure is depicted below:



Prelim. Resp. 3–4. The figure depicts the chemical structure of sofosbuvir with stereochemistry and identifies the compound's phosphoramidate prodrug moiety, modified sugar, and natural uracil base. *Id.* at 4. Claim 16 likewise, in setting forth a compound or stereoisomer of compounds identified by name, including that reproduced above, encompasses the *Sp* stereoisomer, the *Rp* stereoisomer, and mixtures of the two. *Id.* at 3–4, 12; *see also* Pet. 28–29.

D. The Asserted Grounds of Unpatentability

Petitioner contends that “[e]ach and every feature of claims 1, 2, 10-18 and 20-25 can be found in the prior art reference[s] identified below.”¹

¹ Although Petitioner contends “[e]ach and every feature . . . can be found” in the cited references (Pet. 27), the analysis that follows of “exemplary disclosure of the cited references” (*id.*) is effectively limited to consideration of a single compound—the 5'-phosphate (phosphoramidate) prodrug of the uridine analog (2'*R*)-2'-deoxy-2'-fluoro-2'-*C*-methyluridine, wherein the

Pet. 27 (citing Ex. 1002 ¶ 92). More particularly, Petitioner asserts that claims 1, 2, 10–18, and 20–25 are unpatentable based on each of the following grounds. Pet. 3, *see also id.* at 27–55.

References	Statutory Basis
Sofia ²	§ 102
Sofia and Perrone ³	§ 103
Ma ⁴ and Perrone	§ 103

Petitioner supports the Petition with the testimony of Joseph M. Fortunak, Ph.D. (Ex. 1002). Based on Dr. Fortunak's statement of qualifications (*id.* ¶¶ 1–20) and curriculum vitae (Ex. 1003), on this record, we determine that he is qualified to opine from the perspective of a person of ordinary skill in the art.

III. ANALYSIS

A. Level of Skill in the Art

Petitioner contends that a person of ordinary skill in the art would have held either

(1) a Ph.D. in chemistry or a closely related field with some experience in an academic or industrial laboratory focusing on drug discovery or development, and would also have some

5'-phosphate group is the (phenyl)(isopropyl-L-alaninyl)phosphate group (*id.* at 27–55).

² Sofia et al., Poster #P-259, presented at the 14th Int'l Symposium on Hepatitis C Virus and Related Viruses, Glasgow, Scotland, UK, Sept. 9–13, 2007 (Ex. 1004).

³ Perrone et al., 50 J. MED. CHEM. 1840–1849 (2007) (Ex. 1008).

⁴ Ma et al., 282 J. BIOL. CHEM. 29812–29820 (2007) (Ex. 1005).

familiarity with antiviral drugs and their design and mechanism of action, or

(2) a Bachelor's or Master's degree in chemistry or a closely related field with significant experience in an academic or industrial laboratory focusing on drug discovery and/or development for the treatment of viral diseases.

Pet. 5–6 (citing Ex. 1002 ¶ 35).

Patent Owner does not expressly contest the level of ordinary skill.

See generally Prelim. Resp.

On this record, we adopt Petitioner's essentially uncontested definition of the level of ordinary skill. We further note that the prior art itself demonstrates the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that "specific findings on the level of skill in the art . . . [are not required] 'where the prior art itself reflects an appropriate level and a need for testimony is not shown'" (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))).

B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to their broadest reasonable construction in light of the specification of the patent in which they occur. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, we interpret claim terms using "the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's

specification.” *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997). “Under a broadest reasonable interpretation, words of the claim must be given their plain meaning, unless such meaning is inconsistent with the specification and prosecution history.” *Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1062 (Fed. Cir. 2016). If an inventor acts as his or her own lexicographer, the definition must be set forth with reasonable clarity, deliberateness, and precision. *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1249 (Fed. Cir. 1998). Only those term which are in controversy need to be construed and only to the extent necessary to resolve the controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017).

Petitioner contends that “there is no reason to give any of the terms of the claims of the ‘270 [patent] a meaning other than their ordinary and accustomed meaning.” Pet. 6.

Patent Owner does not contest that the claim terms should be given their ordinary and accustomed meaning. *See generally* Prelim. Resp. We determine that no claim term requires express construction for the purpose of determining whether to institute review.

C. Prior Art Status

Under 35 U.S.C. § 311(b), in an *inter partes* review, a petitioner may only challenge the claims of a patent based on “prior art consisting of patents or printed publications,” and the petitioner has the initial burden of producing evidence to support a conclusion of unpatentability under § 102 or § 103, including that an asserted reference is prior art to the challenged claims under a relevant subsection of § 102. “To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory

statements. The petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness.” *In re Magnum Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016).

Petitioner contends that Sofia and Ma are both prior art because the ’315 application does not describe the specific compounds claimed by the ’270 patent in that “it does not discuss the specific compounds and stereochemistry around the phosphorous atom claimed.” Pet. 22; *see also id.* at 24; Ex. 1002 ¶ 72. The relied on declaration evidence, reproduced below in full, states:

The ’315 provisional application does not include a description of the specific compounds claimed by the ’270 patent. While the ’315 provisional discusses broad genera of compounds, it does not discuss the specific compounds and stereochemistry around the phosphorous atom claimed in the ’270 patent.

Ex. 1002 ¶ 72.

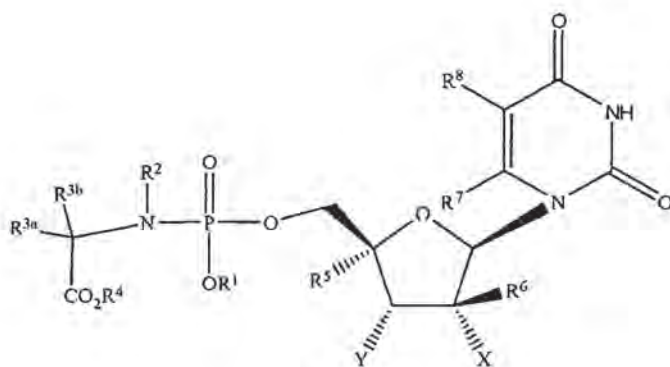
Patent Owner contends the ’270 patent is entitled to the benefit of priority of the ’315 provisional, and that Petitioner wholly fails to meet its burden of producing evidence that the ’270 patent is not entitled to its earliest priority date.⁵ Prelim. Resp. 14–15. Patent Owner contends that “neither [Petitioner] nor its expert has presented a legitimate priority analysis.” *Id.* at 14.

As to the 5'-phosphate (phosphoramidate) prodrug of the uridine analog (2'R)-2'-deoxy-2'-fluoro-2'-C-methyluridine, wherein the 5'-phosphate group is the (phenyl)(isopropyl-L-alaninyl)phosphate group,

⁵ Patent Owner “also submits that the Petition should be stayed pending disposition of the *Oil States* appeal” before the Supreme Court relating to the constitutionality of IPR proceedings. Prelim. Resp. 37–38. The request is moot, however, in light of our decision denying institution.

the focus of Petitioner's anticipation and obviousness analysis (Pet. at 27–55), Patent Owner offers a detailed explanation addressing chemical structure, stereochemistry, and synthesis (Prelim. Resp. 15–19).

Patent Owner relies on the '315 provisional's disclosure of IX-25-2 (Ex. 2013, 195), a compound according to Structure IX (*id.* at 187), in which particular constituents in Structure IX, i.e., R¹, R², R^{3a}, R^{3b}, R⁴, R⁵, R⁶, X, Y, R⁷, and R⁸, are specified in Table IX-25 (*id.* at 195). Patent Owner reproduces Structure IX and Table IX-25 (with emphasis), as depicted below:



IX

Table IX-25.

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

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

Prelim. Resp. at 16–17; *see also* Ex. 2013, 87 (Structure IX), 195 (Table IX-25). Structure IX itself discloses the stereochemistry for most of the structure, but does not depict the stereochemistry at the potentially chiral centers as the carbon substituted with R^{3a} and R^{3b} and at the phosphorus (P).

Patent Owner directs us to disclosure in the '315 provisional that identifies both chiral configurations at the potentially chiral centers at both the carbon substituted with R^{3a} and R^{3b} and at the phosphorus (P) for each compound, including IX-25-2. Prelim Resp. 17–18 (citing Ex. 2013, 63–64). In particular, as to the carbon center, the compounds disclosed by reference to the depicted structures, including Structure IX, and the tables, including Table IX-25, include those in which “ R^{3a} projects towards the viewer while R^{3b} projects away from the viewer” and those in which “ R^{3a} projects away from the viewer while R^{3b} projects towards the viewer.” *Id.* at 17–18 (emphasis omitted) (citing Ex. 2013, 63). And, as to the phosphorus (P), the compounds disclosed includes those in which “the oxo-substituent projects towards the viewer while the OR^1 substituent projects away from the viewer, and vice versa.” *Id.* at 18 (citing Ex. 2013, 63–64).

In sum, the cited disclosure discloses compounds according to IX-25-2 that include both stereochemical orientations at the carbon bearing the specified R^{3a} and R^{3b} constituents, both stereochemical orientations at the phosphorous, and stereochemical orientations elsewhere that are identical to those of sofosbuvir. As such, the cited portions of the '315 provisional constitute disclosure of the Sp stereoisomer (sofosbuvir), as well as the stereoisomers having the opposite stereochemical orientation at either (or both) the carbon bearing R^{3a} and R^{3b} constituents and the phosphorous. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570 (Fed. Cir. 1996) (It is well

settled that “*ipsis verbis* disclosure is not necessary to satisfy the written description requirement of section 112.”); *see also In re Ruschig*, 379 F.2d 990, 994–95 (CCPA 1967) (Analogizing the direction sufficient to identify species in a genus as “blaze marks which single out particular trees.”).

In the face of the '315 provisional's disclosure, including even disclosure of the particular compound relied on in Petitioner's contentions of anticipation and obviousness, we agree with Patent Owner that Petitioner fails to sufficiently demonstrate that the '270 patent is not entitled to the priority benefit of the '315 provisional. We accord little weight to Dr. Fortunak's testimony, because Dr. Fortunak does not identify factual support for his opinion and he fails to address portions of the '315 provisional contrary to his position. *See Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 294 (Fed. Cir. 1985) (“Lack of factual support for expert opinion going to factual determinations” is sufficient to “render the testimony of little probative value in a validity determination.”). Thus, there is no basis for Petitioner's contentions that Sofia is prior art “because it was published by September 13, 2007” (Pet. 22), and that Ma is prior art “because it was published on October 12, 2007” (*id.* at 24).

D. Alleged Unpatentability of the Challenged Claims

1. Anticipation by Sofia

Petitioner asserts that claims 1, 2, 10–18, and 20–25 are anticipated by Sofia. Pet. 27–32. The unavailability of Sofia as prior art undermines Petitioner's anticipation ground. Accordingly, we are not persuaded the record before us establishes a reasonable likelihood that Petitioner will prevail in showing that the subject matter of claims 1, 2, 10–18, and 20–25 is unpatentable over Sofia.

2. *Obviousness over Sofia and Perrone*

Petitioner contends that claims 1, 2, 10–18, and 20–25 are unpatentable as obvious over the combination of Sofia and Perrone. *Id.* at 32–44. The unavailability of Sofia undermines Petitioner’s obviousness ground, which relies on Sofia as to the nucleoside portion of a prodrug according to the claims, that is, “the uridine analog ‘(2’R)-2’-deoxy-2’-fluoro-2’-C-methyluridine.’” *Id.* at 33. Perrone, relied on as to the phosphoramidate portion of the prodrug (*id.* at 37–42), uses a different uridine analog, 4’-azidouridine (Ex. 1008). Accordingly, we are not persuaded the record before us establishes a reasonable likelihood that Petitioner will prevail in showing that the subject matter of claims 1, 2, 10–18, and 20–25 is unpatentable over Sofia and Perrone.

3. *Obviousness over Ma and Perrone*

Petitioner contends that claims 1, 2, 10–18, and 20–25 are unpatentable as obvious over the combination of Ma and Perrone. Pet. 44–55. The unavailability of Ma undermines Petitioner’s obviousness ground, which relies on Ma as to the nucleoside portion of the claimed pro-drug, and on Perrone as to the phosphoramidate portion of the prodrug. *Id.* Accordingly, we are not persuaded the record before us establishes a reasonable likelihood that Petitioner will prevail in showing that the subject matter of claims 1, 2, 10–18, and 20–25 is unpatentable over Ma and Perrone.

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IV. CONCLUSION

Petitioner has not established a reasonable likelihood of prevailing on its assertion that claims 1, 2, 10–18, and 20–25 are unpatentable.

V. ORDER

For the reasons given, it is:

ORDERED that the Petition is *denied* as to all challenged claims of the '270 patent and no trial is instituted.

PETITIONER:

Daniel B Ravicher
RAVICHER LAW FIRM PLLC
dan@ravicher.com

PATENT OWNER:

Dorothy P. Whelan
Michael J. Kane
W. Chad Shear
FISH & RICHARDSON P.C.
whelan@fr.com
kane@fr.com
shear@fr.com

David L. Cavanaugh
Emily R. Whelan
WILMER HALE
david.cavanaugh@wilmerhale.com
emily.whelan@wilmerhale.com

AO 120 (Rev. 08/10)

TO:	Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
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In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the **U.S. District Court for the District of New Jersey** on the following:
 _____ Trademarks or **X** Patents. (_____ the patent action involves 35 U.S.C. § 292.)

DOCKET NO. 3:18-cv-04273-PGS-TJB	DATE FILED 3/27/2018	U.S. DISTRICT COURT TRENTON, NJ
PLAINTIFF GILEAD SCIENCES, INC.		DEFENDANT TEVA PHARMACEUTICALS USA, INC.

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1 7,964,580 B2	06/21/2011	PHARMASSET, INC.
2 8,334,270 B2	12/18/2012	GILEAD PHARMASSET LLC
3 8,580,765 B2	10/12/2013	GILEAD PHARMASSET LLC
4 9,085,573 B2	07/21/2015	GILEAD PHARMASSET LLC
5 7,429,572 B2	9/30/2008	PHARMASSET, INC.

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY _____ Amendment _____ Answer _____ Cross Bill _____ Other Pleading
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK
1	
2	
3	
4	
5	

In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK William T. Walsh	(BY) DEPUTY CLERK s/ John Moller	DATE 3/27/2018
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Copy 1—Upon initiation of action, mail this copy to Director Copy 3—Upon termination of action, mail this copy to Director
 Copy 2—Upon filing document adding patent(s), mail this copy to Director Copy 4—Case file copy

AO 120 (Rev. 08/10)

TO: Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
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In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court _____ of Delaware _____ on the following

☐ Trademarks or ☒ Patents. (☐ the patent action involves 35 U.S.C. § 292.);

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT _____ of Delaware
PLAINTIFF GILEAD SCIENCES, INC. and GILEAD PHARMASSET LLC		DEFENDANT TEVA PHARMACEUTICALS USA, INC. and TEVA PHARMACEUTICAL INDUSTRIES LTD.
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1 7,964,580	6/21/2011	Gilead Pharmasset LLC
2 8,334,270	12/18/2012	Gilead Pharmasset LLC
3 8,580,765	11/12/2013	Gilead Pharmasset LLC
4 9,085,573	7/21/2015	Gilead Pharmasset LLC
5 7,429,572	9/30/2008	Gilead Pharmasset LLC

See attached for additional patents

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1		
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3		
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5		

In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE
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Copy 1—Upon initiation of action, mail this copy to Director Copy 3—Upon termination of action, mail this copy to Director
Copy 2—Upon filing document adding patent(s), mail this copy to Director Copy 4—Case file copy

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
8,415,322	4/9/2013	Gilead Pharmasset LLC
8,633,309	1/21/2014	Gilead Pharmasset LLC
9,284,342	3/15/2016	Gilead Pharmasset LLC
8,618,076	12/31/2013	Gilead Pharmasset LLC
8,889,159	11/18/2014	Gilead Pharmasset LLC
9,549,941	1/24/2017	Gilead Pharmasset LLC
8,629,263	1/14/2014	Gilead Pharmasset LLC
8,735,569	5/27/2014	Gilead Pharmasset LLC
9,637,512	5/2/2017	Gilead Pharmasset LLC
8,642,756	2/4/2014	Gilead Pharmasset LLC
9,206,217	12/8/2015	Gilead Pharmasset LLC
9,340,568	5/17/2016	Gilead Pharmasset LLC