

|              |               |                           |                                             |    |    |
|--------------|---------------|---------------------------|---------------------------------------------|----|----|
| 11           | NPL Documents | Gorbalenya_1989.pdf       | 2635314                                     | no | 11 |
|              |               |                           | 61c01fac0f7ba0120e27a0d72e0b8269521c0ab     |    |    |
| Warnings:    |               |                           |                                             |    |    |
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| 12           | NPL Documents | Grakoui_JViro1_1993.pdf   | 1181642                                     | no | 12 |
|              |               |                           | 4de92e97e17bcd8ba3c735e14b761c3eef8a7       |    |    |
| Warnings:    |               |                           |                                             |    |    |
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| 13           | NPL Documents | Grakoui_ProcNat1_1993.pdf | 1624022                                     | no | 5  |
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| Warnings:    |               |                           |                                             |    |    |
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| 14           | NPL Documents | Griffith_2004.pdf         | 678784                                      | no | 8  |
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| Warnings:    |               |                           |                                             |    |    |
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| 15           | NPL Documents | Halstead_1984.pdf         | 3912578                                     | no | 13 |
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| 16           | NPL Documents | Halstead_1988.pdf         | 999392                                      | no | 7  |
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| 17           | NPL Documents | Hijikata_1993.pdf         | 1298565                                     | no | 11 |
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| 18           | NPL Documents | Jin_1995.pdf              | 719371                                      | no | 7  |
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| 19           | NPL Documents | Kim_1995.pdf              | 360930                                      | no | 7  |
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| Information: |               |                           |                                             |    |    |

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| 20           | NPL Documents | Koonin_1993.pdf  | 3830704                                     | no | 56 |
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| 21           | NPL Documents | Lohmann_1997.pdf | 1773607                                     | no | 13 |
|              |               |                  | 274nc177c357ced82015089749a1d0e9c-III       |    |    |
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| 22           | NPL Documents | Meyers_1996.pdf  | 3437717                                     | no | 35 |
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| 23           | NPL Documents | Moennig_1992.pdf | 2567023                                     | no | 25 |
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| Warnings:    |               |                  |                                             |    |    |
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| 24           | NPL Documents | Monath_1988.pdf  | 458039                                      | no | 4  |
|              |               |                  | 5101c52a2f906db1159d21887c880816d7-639e5    |    |    |
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| 25           | NPL Documents | Ni_2004.pdf      | 3557535                                     | no | 14 |
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| 26           | NPL Documents | Tan_2002.pdf     | 1371353                                     | no | 15 |
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| 27           | NPL Documents | Tomei_1993.pdf   | 948880                                      | no | 10 |
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| 28           | NPL Documents | Walker_2003.pdf  | 3630181                                     | no | 12 |
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| 29                           | NPL Documents | Warrener_1995.pdf   | 631270                                    | no | 7  |
|                              |               |                     | 893154a7701b27b4095220759f322125f7787141  |    |    |
| Warnings:                    |               |                     |                                           |    |    |
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| 30                           | NPL Documents | Wiskerchen_1991.pdf | 1260096                                   | no | 10 |
|                              |               |                     | 882077277168770f884488ef8cc3db46aa7086    |    |    |
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| 31                           | NPL Documents | Xu_1997.pdf         | 1573013                                   | no | 11 |
|                              |               |                     | epd36a5b773d61177b1f0851192704a0d1c039199 |    |    |
| Warnings:                    |               |                     |                                           |    |    |
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| 32                           | NPL Documents | Yuan_1997.pdf       | 566832                                    | no | 5  |
|                              |               |                     | 442e5ca0d515f9ba0d1f131d1001663c62997d    |    |    |
| Warnings:                    |               |                     |                                           |    |    |
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| 33                           | NPL Documents | Zhong_1998.pdf      | 448351                                    | no | 4  |
|                              |               |                     | b88ad9c4fc1ae418256d733c27925cd2104712    |    |    |
| Warnings:                    |               |                     |                                           |    |    |
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| 34                           | NPL Documents | Carroll_2006v2.pdf  | 327369                                    | no | 13 |
|                              |               |                     | 798c910177fcd07c23e8123395f1b142a442dc3e  |    |    |
| Warnings:                    |               |                     |                                           |    |    |
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| 35                           | NPL Documents | Wu_2003v2.pdf       | 821626                                    | no | 13 |
|                              |               |                     | 775d4d0e29e87cc8683e25f8529b0ac94a25c80   |    |    |
| Warnings:                    |               |                     |                                           |    |    |
| Information:                 |               |                     |                                           |    |    |
| Total Files Size (in bytes): |               |                     | 54254178                                  |    |    |

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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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|             |                                     |                 |                  |
|-------------|-------------------------------------|-----------------|------------------|
| Applicant:  | Sofia, et al.                       | Examiner:       | Lewis, Patrick T |
| Serial No.: | 12/053,015                          | Group Art Unit: | 1623             |
| Filed:      | March 21, 2008                      | Docket No.:     | 60137.0034USU1   |
| Title:      | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                 |                  |

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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.

This statement should be considered because it is submitted before the mailing date of a first Office Action on-the-merits. Accordingly, 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." 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

|                                                                                                                                   |                                  |                                   |
|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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|                       | 5538865      | 07-23-1996 | Reyes     |       |          |                            |
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|                       | 5610054      | 03-11-1997 | Draper    |       |          |                            |
|                       | 5633358      | 05-27-1997 | Gruetzke  |       |          |                            |
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|                       | 5676942      | 10-14-1997 | Testa     |       |          |                            |
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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
| EXAMINER                                                                                                                                                                                                                                    | DATE CONSIDERED |
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|                                                                                                                                   |                                  |                                   |
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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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| EXAMINER INITIAL | DOCUMENT NO. | DATE       | NAME       | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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|  | WO 2003051899 | 06-26-2003 | PCT |  |  |  |  |
|  | WO 2003061576 | 07-31-2003 | PCT |  |  |  |  |
|  | WO 2003062256 | 07-31-2003 | PCT |  |  |  |  |
|  | WO 2004002422 | 01-08-2004 | PCT |  |  |  |  |
|  | WO 2004002999 | 01-08-2004 | PCT |  |  |  |  |
|  | WO 2004009610 | 01-29-2004 | PCT |  |  |  |  |
|  | WO 2004080466 | 09-23-2004 | PCT |  |  |  |  |

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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

|  |               |            |     |  |  |  |  |
|--|---------------|------------|-----|--|--|--|--|
|  | WO 2004096234 | 11-11-2004 | PCT |  |  |  |  |
|  | WO 2004096235 | 11-11-2004 | PCT |  |  |  |  |
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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
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|---------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                       | Applicant: Sofia                 |                                   |
|                                                                                                                                       | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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|--|--|--------------------------------------------------------------------------------------------------------------------------|
|  |  | International Search Report for International Application No. PCT/US2004/012472 (WO2005/003147) mailed December 30, 2004 |
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| Electronic Acknowledgement Receipt   |                                     |
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| EFS ID:                              | 7587741                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| Title of Invention:                  | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |
| First Named Inventor/Applicant Name: | MICHAEL JOSEPH SOFIA                |
| Customer Number:                     | 23552                               |
| Filer:                               | Daniel R. Evans/AMY ALBA            |
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| 1               | Foreign Reference    | WO8902733.pdf | 1290840<br><small>8c6bc437180cbe1731d9940357270934370197cc</small> | no               | 33               |

### Warnings:

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| 2            | Foreign Reference | WO9116920.pdf | 1141038                                  | no | 27  |
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| 3            | Foreign Reference | WO9118914.pdf | 2352978                                  | no | 55  |
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| 8            | Foreign Reference | WO9736554.pdf | 786993                                   | no | 24  |
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| 10           | Foreign Reference | WO9822496.pdf | 6130749                                  | no | 132 |
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| 13                  | Foreign Reference | WO9932139.pdf    | 1614715<br>01d7d787e24a6191d48b37a0151a0b7d10/<br>79217 | no | 36  |
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| 19                  | Foreign Reference | WO0037110.pdf    | 1454741<br>11fac01a310036d16da7019e08491c129a72f<br>0ba | no | 33  |
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| 22           | Foreign Reference | WO01060315.pdf | 1712275                                 | no | 51  |
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| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                         |                                                                      |                                                             |    |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                         |                                                                      |                                                             |    |   |
| This is not an USPTO supplied IDS fillable form                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                         |                                                                      |                                                             |    |   |
| <b>Total Files Size (in bytes):</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                         |                                                                      | 178782456                                                   |    |   |
| <p><b>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.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |                                                         |                                                                      |                                                             |    |   |

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 7588027                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 11-MAY-2010                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 13:18:21                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description | File Name    | File Size(Bytes)/<br>Message Digest               | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|--------------|---------------------------------------------------|------------------|------------------|
| 1               | NPL Documents        | Chu_1999.pdf | 655303<br>07c80d199840ca5d5e959724e684b5e92b1d2ed | no               | 4                |

### Warnings:

### Information:

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| 2            | NPL Documents | Chu_1996.pdf           | 707340                                   | no | 4  |
|              |               |                        | 5176d355d1ed27bf6ee41e0d50873ab13g1d17   |    |    |
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| 3            | NPL Documents | DeLombaert_1994.pdf    | 4586851                                  | no | 14 |
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| 4            | NPL Documents | Edmundson_1989.pdf     | 102177                                   | no | 2  |
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| 5            | NPL Documents | Hernandez_JOC_2004.pdf | 163198                                   | no | 8  |
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| 6            | NPL Documents | Hostetler_1992.pdf     | 395877                                   | no | 5  |
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| Information: |               |                        |                                          |    |    |
| 7            | NPL Documents | Kucera_1990.pdf        | 902013                                   | no | 11 |
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| 8            | NPL Documents | Meier_1997.pdf         | 1102483                                  | no | 6  |
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| 11                                                                                                                                                                                                         | NPL Documents | Novak_CCCC_1974.pdf                  | 1028156<br>a7c76e3ab0b0e917326a3e1d0991b1ada9337     | no | 8 |
| Warnings:                                                                                                                                                                                                  |               |                                      |                                                      |    |   |
| The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing |               |                                      |                                                      |    |   |
| Information:                                                                                                                                                                                               |               |                                      |                                                      |    |   |
| 12                                                                                                                                                                                                         | NPL Documents | Novak_CCCC_1971.pdf                  | 570499<br>7ba20000c3d9ac734d63116120b5a180d1149ec    | no | 4 |
| Warnings:                                                                                                                                                                                                  |               |                                      |                                                      |    |   |
| The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing |               |                                      |                                                      |    |   |
| Information:                                                                                                                                                                                               |               |                                      |                                                      |    |   |
| 13                                                                                                                                                                                                         | NPL Documents | Oishi_TL_1993.pdf                    | 197976<br>1e9113796ca1970b124e701fcd0c6ed10eb47ba9   | no | 4 |
| Warnings:                                                                                                                                                                                                  |               |                                      |                                                      |    |   |
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| 14                                                                                                                                                                                                         | NPL Documents | Shih_1994.pdf                        | 447898<br>7ec7776a01317159d30158010eac8f7c8073920b   | no | 8 |
| Warnings:                                                                                                                                                                                                  |               |                                      |                                                      |    |   |
| Information:                                                                                                                                                                                               |               |                                      |                                                      |    |   |
| 15                                                                                                                                                                                                         | NPL Documents | Stella_EOTP_2004.pdf                 | 2363829<br>a091b1545a030e9270eae80b118100ce5a5c7e01e | no | 6 |
| Warnings:                                                                                                                                                                                                  |               |                                      |                                                      |    |   |
| Information:                                                                                                                                                                                               |               |                                      |                                                      |    |   |
| 16                                                                                                                                                                                                         | NPL Documents | Sun_1997.pdf                         | 244162<br>01101472524eae61290123a8f5036a3e54b946d    | no | 5 |
| Warnings:                                                                                                                                                                                                  |               |                                      |                                                      |    |   |
| Information:                                                                                                                                                                                               |               |                                      |                                                      |    |   |
| 17                                                                                                                                                                                                         | NPL Documents | SunXiaoLing_ACS_1996.pdf             | 459068<br>d081c1170c0a2e12758c244828006205a176294    | no | 6 |
| Warnings:                                                                                                                                                                                                  |               |                                      |                                                      |    |   |
| Information:                                                                                                                                                                                               |               |                                      |                                                      |    |   |
| 18                                                                                                                                                                                                         | NPL Documents | ISR_PCTUS2004012472_WO2005003147.pdf | 160230<br>154777005a010016e86b3946467e07870b145      | no | 4 |
| Warnings:                                                                                                                                                                                                  |               |                                      |                                                      |    |   |
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| 19                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | NPL Documents | ISR_PCTUS2005025916_WO2006012440.pdf | 118992<br>d06814001a750d019ca77679b041c7c75e051e    | no | 2 |
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| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |               |                                      |                                                     |    |   |
| 20                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | NPL Documents | ISR_PCTEP2006069060_WO2007065829.pdf | 1304271<br>d1e1baa12ed24339942a9b09ee8831bb3ba066b8 | no | 4 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |               |                                      |                                                     |    |   |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |               |                                      |                                                     |    |   |
| 21                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | NPL Documents | ISR_PCTUS2005032406_WO2006031725.pdf | 131807<br>1fa08c199c9794467f6c15ba003d15d4ff109b31  | no | 3 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |               |                                      |                                                     |    |   |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |               |                                      |                                                     |    |   |
| 22                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | NPL Documents | Bhat_2003v2.pdf                      | 75095<br>202cd080d1a88ee15de65f50508ba9ab0f801      | no | 2 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |               |                                      |                                                     |    |   |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |               |                                      |                                                     |    |   |
| 23                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | NPL Documents | Goekjian_JOC_1999v2.pdf              | 759284<br>bdf6eb889f6da01771e258f1f61c2d22403ce5d   | no | 9 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |               |                                      |                                                     |    |   |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |               |                                      |                                                     |    |   |
| Total Files Size (in bytes):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |               |                                      | 18855600                                            |    |   |
| <p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b>New Applications Under 35 U.S.C. 111</b><br/>If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b>National Stage of an International Application under 35 U.S.C. 371</b><br/>If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b>New International Application Filed with the USPTO as a Receiving Office</b><br/>If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |               |                                      |                                                     |    |   |

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 7588603                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 11-MAY-2010                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 14:08:59                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

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| Submitted with Payment | no |
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### File Listing:

| Document Number | Document Description | File Name              | File Size(Bytes)/<br>Message Digest                  | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|------------------------|------------------------------------------------------|------------------|------------------|
| 1               | Foreign Reference    | WO04096235_p1to497.pdf | 14404454<br>55ee94033ee77d895a30d389ee6d0edd62a0824d | no               | 500              |

### Warnings:

### Information:

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| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Foreign Reference | WO04096235_p498to1155.pdf | 22080418<br>d74c4d077e945134a239aec7c46077916f<br>154584 | no       | 658 |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                   |                           |                                                          |          |     |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                   |                           |                                                          |          |     |
| Total Files Size (in bytes):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                   |                           |                                                          | 36484872 |     |
| <p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/>         If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/>         If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/>         If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |                   |                           |                                                          |          |     |



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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 12/053,015      | 03/21/2008  | MICHAEL JOSEPH SOFIA | 60137.0034USU1      | 3454             |

23552 7596 06/15/2010  
MERCHANT & GOULD PC  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-0903

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| EXAMINER |
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LEWIS, PATRICK T

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| ART UNIT | PAPER NUMBER |
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1623

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| MAIL DATE | DELIVERY MODE |
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06/15/2010

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.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 12/053,015             | SOFIA ET AL.        |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Patrick T. 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 1 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) ☐ 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**

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-12 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ 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).
- 11) ☐ 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**

- 12) ☐ 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) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____                                                          | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
  - I. Claims 1-4 and 11-12, drawn to a compound of formula I, classified in class 536, subclass 22.1.
  - II. Claims 5-8, drawn to the use of a compound of formula I, classified in class 536, subclass 18.5.
  - III. Claims 9-10, drawn to the process of preparing a compound of formula I, classified in class 536, subclass 18.6.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case aspirin can be used to treat a subject in need thereof.
3. Inventions I and III are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product of Invention I could be produced by

the process disclosed by Abraham et al. J. Med. Chem. (1996), Vol. 39, pages 4569-4575. See Scheme 1.

4. Inventions II and III are directed to related processes. The related inventions are distinct if: (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed are not used together, are mutually exclusive and are not obvious variants. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

5. Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

- (a) the inventions have acquired a separate status in the art in view of their different classification;
- (b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;
- (c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

- (d) the prior art applicable to one invention would not likely be applicable to another invention;
- (e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

**Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined** even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable

over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

6. Claims 1-12 are generic to the following disclosed patentably distinct species: a single, specific compound of formula I such as a compound recited in claim 2. The species are independent or distinct because as disclosed the different species have mutually exclusive characteristics for each identified species. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

**Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined** even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(l).

8. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

#### **Contacts**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 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/

|                                   |                                       |                                                            |             |
|-----------------------------------|---------------------------------------|------------------------------------------------------------|-------------|
| <b>Notice of References Cited</b> | Application/Control No.<br>12/053,015 | Applicant(s)/Patent Under<br>Reexamination<br>SOFIA ET AL. |             |
|                                   | Examiner<br>Patrick T. Lewis          | Art Unit<br>1623                                           | Page 1 of 1 |

**U.S. PATENT DOCUMENTS**

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

**FOREIGN PATENT DOCUMENTS**

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

**NON-PATENT DOCUMENTS**

| * |   | Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages) |
|---|---|-------------------------------------------------------------------------------------------|
|   | U | Abraham et al. J. Med. Chem. (1996), Vol. 39, pages 4569-4575.                            |
|   | V |                                                                                           |
|   | W |                                                                                           |
|   | X |                                                                                           |

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



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## BIB DATA SHEET

CONFIRMATION NO. 3454

| SERIAL NUMBER                                                                                                                                                                                                                                                             | FILING or 371(c)<br>DATE                                                                                          | CLASS                                                    | GROUP ART UNIT                    | ATTORNEY DOCKET<br>NO.                                                                                                                                                                                                                                                    |                               |                                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|-------------------------------------|
| 12/053,015                                                                                                                                                                                                                                                                | 03/21/2008                                                                                                        | 514                                                      | 1623                              | 60137.0034USU1                                                                                                                                                                                                                                                            |                               |                                     |
| <b>APPLICANTS</b><br>MICHAEL JOSEPH SOFIA, Doylestown, PA;<br>JINFA DU, New Hope, PA;<br>PEIYUAN WANG, Glen Rock, NJ;<br>DHANAPALAN NAGARATHNAM, Bethany, CT;                                                                                                             |                                                                                                                   |                                                          |                                   |                                                                                                                                                                                                                                                                           |                               |                                     |
| <b>** CONTINUING DATA *****</b><br>This appln claims benefit of 60/909,315 03/30/2007<br>and claims benefit of 60/982,309 10/24/2007                                                                                                                                      |                                                                                                                   |                                                          |                                   |                                                                                                                                                                                                                                                                           |                               |                                     |
| <b>** FOREIGN APPLICATIONS *****</b>                                                                                                                                                                                                                                      |                                                                                                                   |                                                          |                                   |                                                                                                                                                                                                                                                                           |                               |                                     |
| <b>** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** ** SMALL ENTITY **</b><br>05/01/2008                                                                                                                                                                                 |                                                                                                                   |                                                          |                                   |                                                                                                                                                                                                                                                                           |                               |                                     |
| Foreign Priority claimed <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No<br>35 USC 119(a-d) conditions met <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No<br>Verified and /PATRICK T LEWIS/<br>Acknowledged Examiner's Signature |                                                                                                                   | <input type="checkbox"/> Met after Allowance<br>Initials | <b>STATE OR<br/>COUNTRY</b><br>PA | <b>SHEETS<br/>DRAWINGS</b><br>0                                                                                                                                                                                                                                           | <b>TOTAL<br/>CLAIMS</b><br>12 | <b>INDEPENDENT<br/>CLAIMS</b><br>12 |
| <b>ADDRESS</b><br>MERCHANT & GOULD PC<br>P.O. BOX 2903<br>MINNEAPOLIS, MN 55402-0903<br>UNITED STATES                                                                                                                                                                     |                                                                                                                   |                                                          |                                   |                                                                                                                                                                                                                                                                           |                               |                                     |
| <b>TITLE</b><br>NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS                                                                                                                                                                                                                       |                                                                                                                   |                                                          |                                   |                                                                                                                                                                                                                                                                           |                               |                                     |
| <b>FILING FEE<br/>RECEIVED</b><br>2745                                                                                                                                                                                                                                    | FEES: Authority has been given in Paper<br>No. _____ to charge/credit DEPOSIT ACCOUNT<br>No. _____ for following: |                                                          |                                   | <input type="checkbox"/> All Fees<br><input type="checkbox"/> 1.16 Fees (Filing)<br><input type="checkbox"/> 1.17 Fees (Processing Ext. of time)<br><input type="checkbox"/> 1.18 Fees (Issue)<br><input type="checkbox"/> Other _____<br><input type="checkbox"/> Credit |                               |                                     |

|                                                                                                                    |                                            |                                                                |
|--------------------------------------------------------------------------------------------------------------------|--------------------------------------------|----------------------------------------------------------------|
| <b><i>Index of Claims</i></b><br> | <b>Application/Control No.</b><br>12053015 | <b>Applicant(s)/Patent Under Reexamination</b><br>SOFIA ET AL. |
|                                                                                                                    | <b>Examiner</b><br>Patrick T Lewis         | <b>Art Unit</b><br>1623                                        |

|   |                 |   |                   |   |                     |   |                 |
|---|-----------------|---|-------------------|---|---------------------|---|-----------------|
| ✓ | <b>Rejected</b> | - | <b>Cancelled</b>  | N | <b>Non-Elected</b>  | A | <b>Appeal</b>   |
| = | <b>Allowed</b>  | ÷ | <b>Restricted</b> | I | <b>Interference</b> | O | <b>Objected</b> |

| <input type="checkbox"/> Claims renumbered in the same order as presented by applicant |          |            |      |  |  |  |  |  |  |  | <input type="checkbox"/> CPA |  |  |  |  |  |  |  |  |  |  | <input type="checkbox"/> T.D. |  |  |  |  |  |  |  |  |  |  | <input type="checkbox"/> R.1.47 |  |  |  |  |  |  |  |  |  |  |
|----------------------------------------------------------------------------------------|----------|------------|------|--|--|--|--|--|--|--|------------------------------|--|--|--|--|--|--|--|--|--|--|-------------------------------|--|--|--|--|--|--|--|--|--|--|---------------------------------|--|--|--|--|--|--|--|--|--|--|
| CLAIM                                                                                  |          |            | DATE |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
| Final                                                                                  | Original | 06/12/2010 |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
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|                                                                                        | 2        | +          |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
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|                                                                                        | 4        | +          |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
|                                                                                        | 5        | +          |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
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|                                                                                        | 7        | +          |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
|                                                                                        | 8        | +          |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
|                                                                                        | 9        | +          |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
|                                                                                        | 10       | +          |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
|                                                                                        | 11       | +          |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |
|                                                                                        | 12       | +          |      |  |  |  |  |  |  |  |                              |  |  |  |  |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |  |                                 |  |  |  |  |  |  |  |  |  |  |

(FILE 'HOME' ENTERED AT 13:33:12 ON 12 JUN 2010)

FILE 'REGISTRY' ENTERED AT 13:33:28 ON 12 JUN 2010  
L1 STRUCTURE UPLOADED  
L2 50 S L1 SSS SAM  
L3 2103 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 13:34:05 ON 12 JUN 2010  
L4 109 S L3 AND SYNTHESIS

FILE 'STNGUIDE' ENTERED AT 13:36:36 ON 12 JUN 2010



```

chain nodes :
  6  7  8  9 10 11 12 13 14 15 16
ring nodes :
  1  2  3  4  5
chain bonds :
  3-6 5-16 6-7 7-8 8-9 8-10 8-11 9-12 12-13 13-14 13-15
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 5-16 6-7 7-8 8-9 8-10 8-11 9-12 13-14 13-15
exact bonds :
  3-6 12-13
  
```

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Match level :
  1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS
 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom
  
```

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|               |                                     |                   |                   |
|---------------|-------------------------------------|-------------------|-------------------|
| Applicant:    | Michael J. Sofia et al.             | Examiner:         | LEWIS, PATRICK T. |
| Serial No.:   | 12/053,015                          | Group Art Unit:   | 1623              |
| Filed:        | March 21, 2008                      | Docket No.:       | 60137.0034USU1    |
| Customer No.: | 23552                               | Confirmation No.: | 3454              |
| Title:        | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                   |                   |

---

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

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

Dear Sir:

In response to the Restriction Requirement dated June 15, 2010, Applicants elect with traverse the subject matter found in Group I, as applied to the amended claims, for further prosecution. Applicants further elect the species recited in original claim 2, identified as compound 25 or its stereoisomer, with traverse. Applicants request entry of the amendment.

**Amendments to the Claims** begin on page 2 of this paper.

**Remarks** begin on page 7 of this paper.

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

Claims 1-12 (Canceled).

13 (New): (S)-2-([(2R,3R,4R,5R)-5-(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.

14 (New): A composition comprising the compound or a stereoisomer thereof as claimed in claim 13 and a pharmaceutically acceptable medium.

15 (New): A composition for treating a hepatitis C virus, which comprises an effective amount of the compound or a stereoisomer thereof as claimed in claim 13 and a pharmaceutically acceptable medium.

16 (New): A method of treating a subject infected by a virus, which comprises:  
administering to the subject an effective amount of the compound or a stereoisomer thereof as claimed in claim 13;

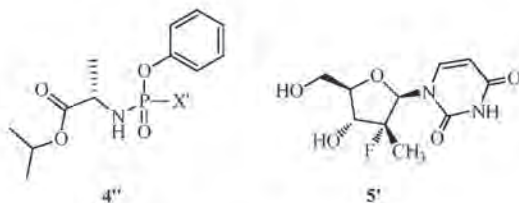
wherein the virus is selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus.

17 (New): A method of treating a hepatitis C virus infection in a subject in need thereof, which comprises:

administering to the subject an effective amount of the compound or a stereoisomer thereof as claimed in claim 13.

18 (New): A process for preparing the compound or a stereoisomer thereof as claimed in claim 13, said process comprising:

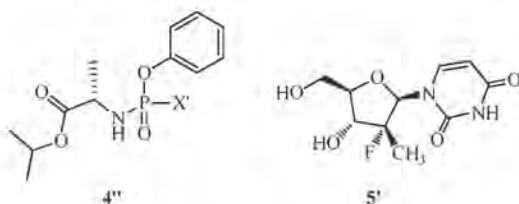
reacting a compound **4''** with a nucleoside analog **5'**



wherein X' is a leaving group.

19 (New): A product comprising the compound or a stereoisomer thereof as claimed in claim 13 obtained by a process comprising:

reacting a compound **4''** with a nucleoside analog **5'**



wherein X' is a leaving group.

20 (New): (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.

21 (New): A composition comprising the compound as claimed in claim 20 and a pharmaceutically acceptable medium.

22 (New): A composition for treating a hepatitis C virus, which comprises an effective amount of the compound as claimed in claim 20 and a pharmaceutically acceptable medium.

23 (New): A method of treating a subject infected by a virus, which comprises:

administering to the subject an effective amount of the compound as claimed in claim 20;

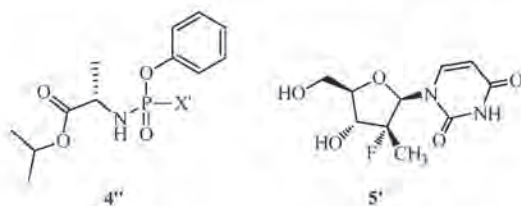
wherein the virus is selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus.

24 (New): A method of treating a 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 claim 20.

25 (New): A process for preparing the compound as claimed in claim 20, said process comprising:

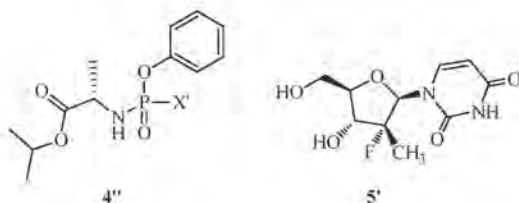
reacting a compound 4'' with a nucleoside analog 5'



wherein X' is a leaving group.

26 (New): A product comprising the compound as claimed in claim 20 obtained by a process comprising:

reacting a compound 4'' with a nucleoside analog 5'



wherein X' is a leaving group.

27 (New): (R)-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.

28 (New): A composition comprising the compound as claimed in claim 27 and a pharmaceutically acceptable medium.

29 (New): A composition for treating a hepatitis C virus, which comprises an effective amount of the compound as claimed in claim 27 and a pharmaceutically acceptable medium.

30 (New): A method of treating a subject infected by a virus, which comprises:

administering to the subject a therapeutically effective amount of the compound as claimed in claim 27;

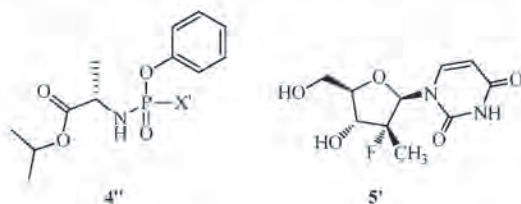
wherein the virus is selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus.

31 (New): A method of treating a 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 claim 27.

32 (New): A process for preparing the compound as claimed in claim 27, said process comprising:

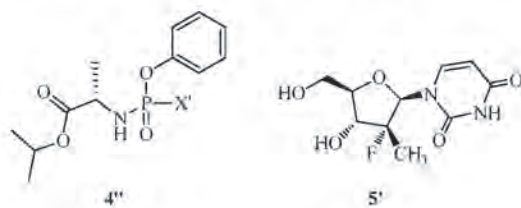
reacting a compound 4'' with a nucleoside analog 5'



wherein X' is a leaving group.

33 (New): A product comprising the compound as claimed in claim 27 obtained by a process comprising:

reacting a compound 4'' with a nucleoside analog 5'



wherein X' is a leaving group.

## **REMARKS**

### **Discussion of Amendments**

Claims 1-12 are canceled without prejudice or disclaimer. Applicants reserve the right to pursue the cancelled subject matter in a subsequent application.

New claims 13-33 are added. Support for new claim 13-33 is summarized below.

| New Claims              | Support                                                                         |
|-------------------------|---------------------------------------------------------------------------------|
| 13, 20, and 27          | Original Claim 2<br>Compound 25<br>(p. 9, ll. 7-10, p. 664,<br>and pp. 674-675) |
| 14-15, 21-22, and 28-29 | Original Claim 4                                                                |
| 16-17, 23-24, and 30-31 | Original Claim 8<br>p. 646, ll. 5-10                                            |
| 18, 25, and 32          | Original Claim 10                                                               |
| 19, 26, and 32          | Original Claim 12                                                               |

No new matter is believed to be added upon entry of the amendment.

### **Restriction Requirement and Species Election**

The Office has required a restriction of the claims as follows:

Group I – Claims 1-4 and 11-12, drawn to a compound of formula I;  
Group II – Claims 5-8, drawn to a use of a compound of formula I; and  
Group III – Claims 9-10, drawn to the process of preparing a compound of formula I.

The Office has also required that Applicants elect a species for further prosecution.

The present amendment cancels claims 1-12. Thus, the restriction requirement is rendered moot because a compound represented by formula I is no longer claimed. Applying the Office's claim grouping to the pending claims provides for the following three groups:

Group I – Claims 13-15, 19, 20-22, 26, 27-29, and 32;  
Group II – Claims 16-17, 23-24, and 30-31; and  
Group III – Claims 18, 25, and 33.

Applicants elect, with traverse, the claims of Group I, as applied to the pending claims.

Claim 13 is directed to (S)-2-[[[(2R,3R,4R,5R)-5-(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 (see chemical structure of compound 25 in the specification at p. 677). As applied to the pending claims, the Group I claims include claims 13-15, 19, 20-22, 26, 27-29, and 32. Applicants believe that the Examiner would not be burdened by searching the subject matter of Groups II and III because a search of the Group I claims would cover the claims of these two groups. A restriction requirement is proper only if the inventions of the restricted groups are either dependent or patentably distinct, and there is a burden in searching the entire application. (MPEP 803) The Applicants believe that a restriction of the claims would be improper here because there would be no serious burden to search the non-elected subject matter. Should the examiner decide to withdraw the non-elected claims of Groups II and III from consideration, the Applicants respectfully request that the non-elected claims be rejoined upon determining that the elected claims are in a condition for allowance (MPEP 806, *In re Ochial*, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995)).

As to the species election, the Applicants elect compound 25 or its stereoisomer thereof, as recited in original claim 2, and presented in new claim 13. Claims 20 and 27, which are two stereoisomers of compound 25, read on the elected species.

#### Information Disclosure Statements

Applicants have concurrently filed an Information Disclosure Statement ("IDS") with the present response. Five of the documents cited there correspond to either a "poster presentation" or "presentation slides," three of which were "published" prior to the filing date of the present application, but after the filing of the provisional applications (60/909,315, filed on March 30, 2007 and 60/982,309, filed on October 24, 2007) for which priority is claimed.<sup>1</sup> The pending claims are adequately supported in the first-filed provisional application (US 60/909,315)

<sup>1</sup> Certain employees of Pharmasset, Inc., the assignee of the present application, published an article related to a 2'-fluoro-2'-methyl-uridine phosphoramidate nucleotide identified there as PSI-7672 (*cf.* Compound 5 in original claim 2) prior to the filing date of the present application. See Murakami et al. Antimicrobial Agents and Chemotherapy (Feb. 2008) 52(2): 458-464. Applicants cited Murakami et al. in the January 14, 2010 IDS at Sheet 2 of 2.

throughout the specification and specifically at page 195, Table IX-25, Compound No. IX-25-2. Acknowledgement of Applicants' claim to priority is respectfully requested.

One document cited in the concurrently filed IDS relates to a response filed in the EPO on October 25, 2010 ("EPO Response") for the corresponding European patent application (EP08732818.3). The EPO Response included an amendment with claims that are similar to those found in the present application. The EPO Response also included remarks that addressed the Written Opinion made for the corresponding PCT application (PCT/US2008/058183).<sup>2</sup> The PCT Written Opinion stated at Box No. V that claim 2 was found to be novel over the following references: **D1**: WO 2006/012078; **D2**: WO 2006/065335; **D3**: Gunic et al. Bioorg. & Med. Chem. Letters (2007) 17(9): 2456-2458; **D4**: US 6475985; **D5**: WO 03/000713; **D6**: WO 2005/012327; **D7**: WO 2007/020193; **D8**: US 2006/0241064; **D9**: WO 2005/003147; and **D10**: WO 2007/095269. Moreover, the PCT Written Opinion provided reasons why claim 2 was not inventive over **D8** and **D9** (see Section "Re Item V"). In the EPO Response, reasons were provided at pp. 3-7 why the claimed subject matter is inventive over **D8** and **D9**. The EPO Response cites at page 6 of the EPO Response (J.L. Clark et al. J. Med. Chem. (2005) 48(17): 5504-5508). Applicants cited that reference in the IDS filed April 29, 2010 (see Sheet 7 of 9).

In addition to the concurrently filed IDS, Applicants have filed six other IDSs in the present application on: January 14, 2010; March 18, 2010; April 29, 2010; April 30, 2010; May 4, 2010; and May 11, 2010. Applicants respectfully request that the Examiner consider the cited references. Applicants also request that in the next Office communication, the Examiner provide an indication that each one of the cited references has been considered.

## Conclusion

Applicants believe that the amended claims are in a condition for allowance.

In the event that the Examiner discovers an informal matter that can be discussed by telephone, the Examiner is invited to contact Applicants' representative in order to expedite prosecution in the present application. No additional fee is believed to be due; however, the

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<sup>2</sup>The Applicants cited the PCT Written Opinion and references cited therein in an IDS filed April 30, 2010.

U.S. Patent Application No. 12/053,015  
Response to Restriction Requirement dated June 15, 2010

Director is hereby authorized to charge any fees that may be required or credit any overpayment to Deposit Account 13-2725.



Dated: October 28, 2010

Respectfully submitted,

MERCHANT & GOULD P.C.  
P.O. Box 2903  
Minneapolis, Minnesota 55402-0903  
(612) 332-5300

By /Daniel R. Evans/  
Daniel R. Evans  
Reg. No. 55,868

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|             |                                     |                 |                  |
|-------------|-------------------------------------|-----------------|------------------|
| Applicant:  | Sofia et al.                        | Examiner:       | Lewis, Patrick T |
| Serial No.: | 12/053,015                          | Group Art Unit: | 1623             |
| Filed:      | March 21, 2008                      | Docket No.:     | 60137.0034USU1   |
| 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.

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

In accordance with 37 C.F.R. § 1.98(a)(2), a copy of each foreign patent and/or a copy of each publication, other than U.S. patents and U.S. patent application publications, listed on the accompanying Form 1449 is enclosed.

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." 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.

If fees are required for consideration of the items listed on the enclosed Form 1449, please charge such fees 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

|                                                                                                                                       |                                  |                                   |
|---------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                       | Applicant: Sofia et al.          |                                   |
|                                                                                                                                       | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| U.S. PATENT DOCUMENTS |              |      |      |       |          |                            |
|-----------------------|--------------|------|------|-------|----------|----------------------------|
| EXAMINER INITIAL      | DOCUMENT NO. | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                       |              |      |      |       |          |                            |

| U.S. PUBLISHED PATENT APPLICATION |              |      |      |       |          |                            |
|-----------------------------------|--------------|------|------|-------|----------|----------------------------|
| EXAMINER INITIAL                  | DOCUMENT NO. | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                                   |              |      |      |       |          |                            |
|                                   |              |      |      |       |          |                            |

| FOREIGN PATENT DOCUMENTS |              |      |         |       |          |             |    |
|--------------------------|--------------|------|---------|-------|----------|-------------|----|
|                          | DOCUMENT NO. | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION |    |
|                          |              |      |         |       |          | YES         | NO |
|                          |              |      |         |       |          |             |    |
|                          |              |      |         |       |          |             |    |

| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |  |                                                                                                                                                                                                                                                                                          |
|------------------------------------------------------------------------|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                        |  | Pogam et al., "No Evidence of R7128 Drug Resistance After Up to 4 Weeks Treatment of GT1, 2 and 3 Hepatitis C Virus Infected Individuals", from 44th Annual Meeting of European Association for the Study of the Liver (EASL), Copenhagen, Denmark Apr 22 - Apr 26, 2009                 |
|                                                                        |  | Sofia et al., "β-D2'-Deoxy-2'-C-methyluridine Phosphoramidates: Potent and Selective Inhibitors of HCV RNA Replication", Poster # P-259, presented at the 14 <sup>th</sup> International Symposium on Hepatitis C Virus and Related Viruses, Glasgow, Scotland, UK, September 9-13, 2007 |
|                                                                        |  | Sofia, "β-D-2'-Deoxy-2'-fluoro-2'-C-methyluridine Phosphoramidates: Potent and Selective Inhibitors of HCV RNA Replication", 2nd International Workshop on HCV - Resistance and New Compounds, October 31, 2007                                                                          |
|                                                                        |  | Sofia et al., "β-D-2'-Deoxy-2'-fluoro-2'-C-methyluridine Phosphoramidates: Potent and Selective Inhibitors of HCV RNA Replication", 2nd International Workshop on HCV", Poster #7, October 31, 2007                                                                                      |
|                                                                        |  | Sofia et al., "R7128, A Potent and Selective Nucleoside Inhibitor of HCV NS5B Polymerase: An Overview of Clinical Efficacy and Progress Toward Second Generation Inhibitors", From HCV Drug Discovery 2008, Chicago, IL, April 28, 2008                                                  |
|                                                                        |  | Response filed October 25, 2010 at the EPO for European patent application no. EP08732818.3                                                                                                                                                                                              |

|                                                                                                                                                                                                                                             |                 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| <b>23552</b><br>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 Patent Application Fee Transmittal |          |                                     |        |                      |
|-----------------------------------------------|----------|-------------------------------------|--------|----------------------|
| Application Number:                           |          | 12053015                            |        |                      |
| Filing Date:                                  |          | 21-Mar-2008                         |        |                      |
| Title of Invention:                           |          | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |        |                      |
| First Named Inventor/Applicant Name:          |          | MICHAEL JOSEPH SOFIA                |        |                      |
| Filer:                                        |          | Daniel R. Evans/AMY ALBA            |        |                      |
| Attorney Docket Number:                       |          | 60137.0034USU1                      |        |                      |
| Filed as Small 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 - 4 months with \$0 paid            | 2254     | 1                                   | 865    | 865                  |

| Description       | Fee Code | Quantity | Amount | Sub-Total in USD(\$) |
|-------------------|----------|----------|--------|----------------------|
| Miscellaneous:    |          |          |        |                      |
| Total in USD (\$) |          |          |        | 865                  |

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 8721427                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 28-OCT-2010                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 13:37:36                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                                                                                                                                                                                                                                                                                                                                                     |                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| Submitted with Payment                                                                                                                                                                                                                                                                                                                              | yes             |
| Payment Type                                                                                                                                                                                                                                                                                                                                        | Credit Card     |
| Payment was successfully received in RAM                                                                                                                                                                                                                                                                                                            | \$ 865          |
| RAM confirmation Number                                                                                                                                                                                                                                                                                                                             | 9875            |
| Deposit Account                                                                                                                                                                                                                                                                                                                                     | 132725          |
| Authorized User                                                                                                                                                                                                                                                                                                                                     | EVANS,DANIEL R. |
| <p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)</p> |                 |

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               | Extension of Time                                    | 12053015_4MoEOT_60137_0034usu1.pdf             | 57461<br>a111d0b1277ce09c/809301830811591d098b50556 | no               | 1                |
| Warnings:       |                                                      |                                                |                                                     |                  |                  |
| Information:    |                                                      |                                                |                                                     |                  |                  |
| 2               | Authorization for Extension of Time all replies      | 12053015_AUTH_allReplies_60137_0034usu1.pdf    | 71327<br>a19288f332ce346730c1dd05801edd108b6429     | no               | 1                |
| Warnings:       |                                                      |                                                |                                                     |                  |                  |
| Information:    |                                                      |                                                |                                                     |                  |                  |
| 3               |                                                      | 12053015_Response_061510R_R_60137_0034usu1.pdf | 120180<br>10c887a7d75243940400a0220032cd0f5647388b  | yes              | 10               |
|                 | Multipart Description/PDF files in .zip description  |                                                |                                                     |                  |                  |
|                 | Document Description                                 | Start                                          |                                                     | End              |                  |
|                 | Response to Election / Restriction Filed             | 1                                              |                                                     | 1                |                  |
|                 | Claims                                               | 2                                              |                                                     | 6                |                  |
|                 | Applicant Arguments/Remarks Made in an Amendment     | 7                                              |                                                     | 10               |                  |
| Warnings:       |                                                      |                                                |                                                     |                  |                  |
| Information:    |                                                      |                                                |                                                     |                  |                  |
| 4               |                                                      | 12053015_IDS_PTO1449_091510_60137_0034usu1.pdf | 121050<br>816652300a6a60d0d090710e991652106c577402  | yes              | 2                |
|                 | Multipart Description/PDF files in .zip description  |                                                |                                                     |                  |                  |
|                 | Document Description                                 | Start                                          |                                                     | End              |                  |
|                 | Transmittal Letter                                   | 1                                              |                                                     | 1                |                  |
|                 | Information Disclosure Statement (IDS) Filed (SB/08) | 2                                              |                                                     | 2                |                  |
| Warnings:       |                                                      |                                                |                                                     |                  |                  |
| Information:    |                                                      |                                                |                                                     |                  |                  |
| 5               | NPL Documents                                        | Sofia_HCV_Workshop_103107.pdf                  | 413773<br>9750c0d0a0886b3d0f6e07f655bce3ee0a640     | no               | 15               |
| Warnings:       |                                                      |                                                |                                                     |                  |                  |
| Information:    |                                                      |                                                |                                                     |                  |                  |

|                              |                         |                                          |                                                      |    |    |
|------------------------------|-------------------------|------------------------------------------|------------------------------------------------------|----|----|
| 6                            | NPL Documents           | EP087328183_Response_filed_102510_v2.pdf | 181418<br>23ed902ee1/c18f0e0a396b613145ae232e31f9d   | no | 15 |
| Warnings:                    |                         |                                          |                                                      |    |    |
| Information:                 |                         |                                          |                                                      |    |    |
| 7                            | NPL Documents           | Pogam_2009_v2.pdf                        | 107809<br>008ba11ca816b9b9479eeb27c3b6c5a0351146e4ec | no | 1  |
| Warnings:                    |                         |                                          |                                                      |    |    |
| Information:                 |                         |                                          |                                                      |    |    |
| 8                            | NPL Documents           | Sofia_Poster259_14thIntHCV_090907_v2.pdf | 74083<br>e94f0c1151f716ada7a0a22127086a81890a6e0d2   | no | 1  |
| Warnings:                    |                         |                                          |                                                      |    |    |
| Information:                 |                         |                                          |                                                      |    |    |
| 9                            | NPL Documents           | Sofia_HCVWorkshop_Poster7_103107_v2.pdf  | 72856<br>7d8d9881ca7b18958e10a885c1ee21e1c5397775    | no | 1  |
| Warnings:                    |                         |                                          |                                                      |    |    |
| Information:                 |                         |                                          |                                                      |    |    |
| 10                           | NPL Documents           | Sofia_Chicago_2008_v2.pdf                | 978483<br>de16e7e2a20b17d6f3440cc197756b028b64c92a   | no | 35 |
| Warnings:                    |                         |                                          |                                                      |    |    |
| Information:                 |                         |                                          |                                                      |    |    |
| 11                           | Fee Worksheet (PTO-875) | fee-info.pdf                             | 30426<br>7c3d01f21c2a5971ff0d3ee35ee0fc38a58d680     | no | 2  |
| Warnings:                    |                         |                                          |                                                      |    |    |
| Information:                 |                         |                                          |                                                      |    |    |
| Total Files Size (in bytes): |                         |                                          | 2228866                                              |    |    |

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, Patrick T |
| Serial No.: | 12/053,015                          | Group Art Unit: | 1623             |
| Filed:      | March 21, 2008                      | Docket No.:     | 60137.0034USU1   |
| Title:      | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                 |                  |

---

REQUEST FOR EXTENSION OF TIME

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

Dear Sir:

In accordance with the provisions of 37 C.F.R. §1.136(a), it is respectfully requested that a four-month extension of time be granted in which to respond to the outstanding Restriction Requirement mailed June 15, 2010, said period of response being extended from July 15, 2010 to November 15, 2010.

Please charge \$865.00 extension of time fee for a small entity and any additional fees or credit overpayment to Deposit Account No. 13-2725.

Respectfully submitted,

MERCHANT & GOULD P.C.  
P.O. Box 2903  
Minneapolis, Minnesota 55402-0903  
(612) 332-5300



By /Daniel R. Evans/  
Daniel R. Evans  
Reg. No. 55,868

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|             |                                     |                 |                  |
|-------------|-------------------------------------|-----------------|------------------|
| Applicant:  | Sofia et al.                        | Examiner:       | Lewis, Patrick T |
| Serial No.: | 12/053,015                          | Group Art Unit: | 1623             |
| Filed:      | March 21, 2008                      | Docket No.:     | 60137.0034USU1   |
| Title:      | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                 |                  |

---

**AUTHORIZATION FOR EXTENSION OF TIME ALL REPLIES**

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

Dear Sir:

Please consider this a petition for extension of time for a sufficient number of months to enter these papers or any future papers, if appropriate. Please consider this automatic authorization to charge fees to address fees required by requests for extensions of time under 37 CFR 1.136

Please further charge any additional fees required to enter these papers or any future papers, or credit any overpayment of fees, to Deposit Account No. 13-2725.



MERCHANT & GOULD P.C.  
P.O. Box 2903  
Minneapolis, Minnesota 55402-0903  
(612) 332-5300

By /Daniel R. Evans/  
Daniel R. Evans  
Reg. No. 55,868

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.

| <b>PATENT APPLICATION FEE DETERMINATION RECORD</b><br>Substitute for Form PTO-875                                               |                                                                                                                                                                                                                                |                                  |            |                                    | Application or Docket Number<br><b>12/053,015</b> |                                                  | Filing Date<br><b>03/21/2008</b> |          | <input type="checkbox"/> To be Mailed |                         |                     |
|---------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|------------|------------------------------------|---------------------------------------------------|--------------------------------------------------|----------------------------------|----------|---------------------------------------|-------------------------|---------------------|
| <b>APPLICATION AS FILED – PART I</b>                                                                                            |                                                                                                                                                                                                                                |                                  |            |                                    |                                                   |                                                  |                                  |          |                                       |                         |                     |
| (Column 1)                                                                                                                      |                                                                                                                                                                                                                                |                                  | (Column 2) |                                    |                                                   | SMALL ENTITY <input checked="" type="checkbox"/> |                                  | OR       |                                       | OTHER THAN SMALL ENTITY |                     |
| FOR                                                                                                                             | NUMBER FILED                                                                                                                                                                                                                   | NUMBER EXTRA                     | RATE (\$)  | FEE (\$)                           |                                                   |                                                  | RATE (\$)                        | FEE (\$) |                                       |                         |                     |
| <input type="checkbox"/> BASIC FEE<br>(37 CFR 1.16(a), (b), or (c))                                                             | N/A                                                                                                                                                                                                                            | N/A                              | N/A        |                                    |                                                   |                                                  | N/A                              |          |                                       |                         |                     |
| <input type="checkbox"/> SEARCH FEE<br>(37 CFR 1.16(k), (l), or (m))                                                            | N/A                                                                                                                                                                                                                            | N/A                              | N/A        |                                    |                                                   |                                                  | N/A                              |          |                                       |                         |                     |
| <input type="checkbox"/> EXAMINATION FEE<br>(37 CFR 1.16(o), (p), or (q))                                                       | N/A                                                                                                                                                                                                                            | N/A                              | N/A        |                                    |                                                   |                                                  | N/A                              |          |                                       |                         |                     |
| TOTAL CLAIMS<br>(37 CFR 1.16(i))                                                                                                | minus 20 = *                                                                                                                                                                                                                   |                                  | X \$ =     |                                    | OR                                                |                                                  | X \$ =                           |          |                                       |                         |                     |
| INDEPENDENT CLAIMS<br>(37 CFR 1.16(h))                                                                                          | minus 3 = *                                                                                                                                                                                                                    |                                  | X \$ =     |                                    | OR                                                |                                                  | X \$ =                           |          |                                       |                         |                     |
| <input type="checkbox"/> APPLICATION SIZE FEE<br>(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). |                                  |            |                                    |                                                   |                                                  |                                  |          |                                       |                         |                     |
| <input type="checkbox"/> 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                            |          |                                       |                         |                     |
| <b>APPLICATION AS AMENDED – PART II</b>                                                                                         |                                                                                                                                                                                                                                |                                  |            |                                    |                                                   |                                                  |                                  |          |                                       |                         |                     |
| (Column 1)                                                                                                                      |                                                                                                                                                                                                                                |                                  | (Column 2) |                                    |                                                   | SMALL ENTITY                                     |                                  | OR       |                                       | OTHER THAN SMALL ENTITY |                     |
| <b>AMENDMENT</b>                                                                                                                | <b>10/28/2010</b>                                                                                                                                                                                                              | CLAIMS REMAINING AFTER AMENDMENT |            | HIGHEST NUMBER PREVIOUSLY PAID FOR | PRESENT EXTRA                                     | RATE (\$)                                        | ADDITIONAL FEE (\$)              |          |                                       | RATE (\$)               | ADDITIONAL FEE (\$) |
|                                                                                                                                 | Total (37 CFR 1.16(g))                                                                                                                                                                                                         | * 21                             | Minus      | ** 20                              | = 1                                               | X \$26 =                                         | 26                               | OR       |                                       | X \$ =                  |                     |
|                                                                                                                                 | Independent (37 CFR 1.16(h))                                                                                                                                                                                                   | * 4                              | Minus      | *** 12                             | = 0                                               | X \$110 =                                        | 0                                | OR       |                                       | X \$ =                  |                     |
|                                                                                                                                 | <input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))                                                                                                                                                                 |                                  |            |                                    |                                                   |                                                  |                                  | OR       |                                       |                         |                     |
|                                                                                                                                 | <input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))                                                                                                                                       |                                  |            |                                    |                                                   |                                                  |                                  | OR       |                                       |                         |                     |
|                                                                                                                                 |                                                                                                                                                                                                                                |                                  |            |                                    |                                                   | TOTAL ADD'L FEE                                  | <b>26</b>                        | OR       |                                       | TOTAL ADD'L FEE         |                     |
| <b>AMENDMENT</b>                                                                                                                |                                                                                                                                                                                                                                | CLAIMS REMAINING AFTER AMENDMENT |            | HIGHEST NUMBER PREVIOUSLY PAID FOR | PRESENT EXTRA                                     | RATE (\$)                                        | ADDITIONAL FEE (\$)              |          |                                       | RATE (\$)               | ADDITIONAL FEE (\$) |
|                                                                                                                                 | Total (37 CFR 1.16(g))                                                                                                                                                                                                         | *                                | Minus      | **                                 | =                                                 | X \$ =                                           |                                  | OR       |                                       | X \$ =                  |                     |
|                                                                                                                                 | Independent (37 CFR 1.16(h))                                                                                                                                                                                                   | *                                | Minus      | ***                                | =                                                 | X \$ =                                           |                                  | OR       |                                       | X \$ =                  |                     |
|                                                                                                                                 | <input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))                                                                                                                                                                 |                                  |            |                                    |                                                   |                                                  |                                  | OR       |                                       |                         |                     |
|                                                                                                                                 | <input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))                                                                                                                                       |                                  |            |                                    |                                                   |                                                  |                                  | OR       |                                       |                         |                     |
|                                                                                                                                 |                                                                                                                                                                                                                                |                                  |            |                                    |                                                   | TOTAL ADD'L FEE                                  |                                  | OR       |                                       | TOTAL ADD'L FEE         |                     |
| * If the entry in column 1 is less than the entry in column 2, write "0" in column 3.                                           |                                                                                                                                                                                                                                |                                  |            |                                    |                                                   |                                                  |                                  |          |                                       |                         |                     |
| ** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".                                       |                                                                                                                                                                                                                                |                                  |            |                                    |                                                   |                                                  |                                  |          |                                       |                         |                     |
| *** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".                                        |                                                                                                                                                                                                                                |                                  |            |                                    |                                                   |                                                  |                                  |          |                                       |                         |                     |
| The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1. |                                                                                                                                                                                                                                |                                  |            |                                    |                                                   |                                                  |                                  |          |                                       |                         |                     |

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

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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                       | Applicant: Sofia et al.          |                                   |
|                                                                                                                                       | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| U.S. PATENT DOCUMENTS |              |            |       |       |          |                            |
|-----------------------|--------------|------------|-------|-------|----------|----------------------------|
| EXAMINER INITIAL      | DOCUMENT NO. | DATE       | NAME  | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                       | 3852267      | 12-03-1974 | Meyer |       |          |                            |
|                       |              |            |       |       |          |                            |
|                       |              |            |       |       |          |                            |

| U.S. PUBLISHED PATENT APPLICATION |              |      |      |       |          |                            |
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| FOREIGN PATENT DOCUMENTS |               |            |         |       |          |               |    |
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|                          | DOCUMENT NO.  | DATE       | COUNTRY | CLASS | SUBCLASS | TRANSLATION   |    |
|                          |               |            |         |       |          | YES           | NO |
|                          | JP 5238939    | 09-17-1993 | JP      |       |          | Abstract only | X  |
|                          | WO 03104250   | 12-18-2003 | PCT     |       |          |               |    |
|                          | WO 2005082144 | 09-09-2005 | PCT     |       |          |               |    |
|                          | WO 2006031725 | 03-23-2006 | PCT     |       |          |               |    |
|                          | WO 2007027248 | 03-08-2007 | PCT     |       |          |               |    |
|                          | WO 2007065829 | 06-14-2007 | PCT     |       |          |               |    |
|                          | CN 101108870  | 01-23-2008 | CN      |       |          | Abstract only | X  |
|                          | WO 2008045419 | 04-17-2008 | PCT     |       |          |               |    |
|                          | WO 2009152095 | 12-17-2009 | PCT     |       |          |               |    |
|                          | WO 2010075554 | 07-01-2010 | PCT     |       |          |               |    |
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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia et al.          |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |                                                                                                                                              |
|------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                        | Baschang et al., Angewandte Chemie, 85:1, 44-45, 1973                                                                                        |
|                                                                        | Broeders et al., J. Am. Chem. Soc., 112:21, 7475-7482, 1990                                                                                  |
|                                                                        | Engels et al., Chem. Ber., 110:6, 2019-2027, 1977                                                                                            |
|                                                                        | Lopez Aparicio et al., "Branched-Chain Sugars, Part VII, Synthesis of Saccharinic Acid Derivatives" Carbohydrate Research, 129, 99-109, 1984 |
|                                                                        | Nelson et al., J. Am. Chem. Soc., 109:13, 4058-4064, 1987                                                                                    |
|                                                                        | Written Opinion of PCT/US2004/012472 mailed December 30, 2004                                                                                |
|                                                                        | International Preliminary Examination Report of PCT/US2004/012472 issued December 1, 2005                                                    |
|                                                                        | Written Opinion of PCT/US2005/025916 mailed June 15, 2006                                                                                    |
|                                                                        | International Preliminary Examination Report of PCT/US2005/025916 issued January 23, 2007                                                    |
|                                                                        | Supplemental European Search Report of European patent appln no. EP 05775359.2 dated September 15, 2010                                      |
|                                                                        | Written Opinion of PCT/US2005/032406 mailed May 8, 2008                                                                                      |
|                                                                        | International Preliminary Examination Report of PCT/US2005/032406 issued March 10, 2009                                                      |
|                                                                        | Written Opinion of PCT/EP2006/069060 mailed January 30, 2007                                                                                 |
|                                                                        | International Preliminary Examination Report of PCT/EP2006/069060 mailed November 5, 2008                                                    |
|                                                                        | Written Opinion of PCT/US2008/058183 mailed March 31, 2010                                                                                   |
|                                                                        | International Search Report of PCT/US2009/046619 (WO/2009/152095) mailed September 23, 2010                                                  |
|                                                                        | Partial International Search Report of PCT/US2009/069475 (WO/2010/075554) mailed March 5, 2010                                               |
|                                                                        | Final International Report and Written Opinion of PCT/US2009/069475 mailed May 10, 2010                                                      |
|                                                                        | Invitation to Pay Additional Fees & Partial International Search Report of PCT/US2010/035641 mailed July 23, 2010                            |
|                                                                        | International Search Report of PCT/US2010/035641 mailed September 28, 2010                                                                   |
|                                                                        | Written Opinion of PCT/US2010/035641 mailed September 28, 2010                                                                               |

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| EFS ID:                              | 8865511                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 18-NOV-2010                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 13:34:20                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

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| Document Number | Document Description | File Name                                              | File Size(Bytes)/<br>Message Digest               | Multi Part /.zip | Pages (if appl.) |
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| 1               |                      | 12053015_IDS_PTO1449_RelatedAppIn_3_60137_0034usu1.pdf | 107629<br>6328f9465b2274ccbf71009fed1660ea3090ed2 | yes              | 3                |

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| Warnings:    |                                                      |                    |                                                     |     |     |
| Information: |                                                      |                    |                                                     |     |     |
| 2            | Foreign Reference                                    | JP5238939A.pdf     | 331651<br>a41896604770aa9752355c43e0c9f5aef2718ba8c | no  | 7   |
| Warnings:    |                                                      |                    |                                                     |     |     |
| Information: |                                                      |                    |                                                     |     |     |
| 3            | Foreign Reference                                    | WO2005082144A1.pdf | 2345875<br>5520e5112ae46d1987006f8c2e297f008f7108a  | no  | 64  |
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| 4            | Foreign Reference                                    | WO2006031725A2.pdf | 2726445<br>a0f1a6a4a00a33433d490aa765a35968b9c7fc   | no  | 74  |
| Warnings:    |                                                      |                    |                                                     |     |     |
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| 5            | Foreign Reference                                    | WO2007027248A2.pdf | 5695548<br>2542ebf3ba6157db6c1d6470ac859115204e7db0 | no  | 158 |
| Warnings:    |                                                      |                    |                                                     |     |     |
| Information: |                                                      |                    |                                                     |     |     |
| 6            | Foreign Reference                                    | WO2007065829A1.pdf | 2090341<br>aa27c0a0b1f020e5d5dc3e97f8a2ef3e448633   | no  | 44  |
| Warnings:    |                                                      |                    |                                                     |     |     |
| Information: |                                                      |                    |                                                     |     |     |
| 7            | Foreign Reference                                    | CN101108870A.pdf   | 417690<br>3e0f3102a9140f12a444e0361f00ba80885c1044  | no  | 13  |
| Warnings:    |                                                      |                    |                                                     |     |     |
| Information: |                                                      |                    |                                                     |     |     |
| 8            | Foreign Reference                                    | WO2008045419A1.pdf | 851396<br>8c2b7261d07f6f631e4466a4461637a2425f29e4  | no  | 24  |
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| 9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | NPL Documents | Baschang_1973.PDF | 144142<br>93284db28b553e724d7592e01f687f4796f8e7    | no | 2  |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                   |                                                     |    |    |
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| 10                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | NPL Documents | Broeders_1990.PDF | 916757<br>14c29cb318f6e1c60809b24c945ca294d65580    | no | 8  |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                   |                                                     |    |    |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                   |                                                     |    |    |
| 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | NPL Documents | Engels_1977.PDF   | 423170<br>079467a02d81f9aef7ddc036cd3d9882c4c08b0   | no | 10 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                   |                                                     |    |    |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                   |                                                     |    |    |
| 12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | NPL Documents | Lopez_1984.pdf    | 609143<br>2d886f9b5776113cb1c287c5eeb65d07e086      | no | 11 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                   |                                                     |    |    |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                   |                                                     |    |    |
| 13                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | NPL Documents | Nelson_1987.PDF   | 697091<br>b59ee2f080eac4f87a15c0f8ce1725035b7c0270e | no | 8  |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                   |                                                     |    |    |
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| <p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/>If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/>If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/>If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |               |                   |                                                     |    |    |

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|             |                                     |                 |                  |
|-------------|-------------------------------------|-----------------|------------------|
| Applicant:  | Sofia et al.                        | Examiner:       | Lewis, Patrick T |
| Serial No.: | 12/053,015                          | Group Art Unit: | 1623             |
| Filed:      | March 21, 2008                      | Docket No.:     | 60137.0034USU1   |
| 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.

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

In accordance with 37 C.F.R. § 1.98(a)(2), a copy of each foreign patent and/or a copy of each publication, other than U.S. patents and U.S. patent application publications, listed on the accompanying Form 1449 is enclosed.

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." 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.

If fees are required for consideration of the items listed on the enclosed Form 1449, please charge such fees 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

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

REC'D 29 DEC 2004

WIPO

PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/US2004/012472

International filing date (day/month/year)  
21.04.2004

Priority date (day/month/year)  
30.05.2003

International Patent Classification (IPC) or both national classification and IPC  
C07H19/06, C07H19/16, C07H19/14, A61K31/7064, A61K31/7076, A61P31/12

Applicant  
PHARMASSET, INC.

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl  
Fax: +31 70 340 - 3016

Authorized Officer

de Nooy, A

Telephone No. +31 70 340-2338



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/012472

**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/012472

---

**Box No. II Priority**

---

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/012472

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 31-126 (in part)

because:

- ☒ the said international application, or the said claims Nos. 31-126 (in part) relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
  - the written form ☐ has not been furnished
  - ☐ does not comply with the standard
  - the computer readable form ☐ has not been furnished
  - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/012472

---

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

|                               |             |               |
|-------------------------------|-------------|---------------|
| Novelty (N)                   | Yes: Claims | 1-130         |
|                               | No: Claims  |               |
| Inventive step (IS)           | Yes: Claims | 1-130         |
|                               | No: Claims  |               |
| Industrial applicability (IA) | Yes: Claims | 1-30, 127-130 |
|                               | No: Claims  |               |

2. Citations and explanations

**see separate sheet**

**Re Item III.**

Claims 31-126 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

For the assessment of the present claims 31-126 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Item V.**

- 1 The following document is referred to in this communication:  
D1 : US 2003/060400 A1 (LACOLLA PAULO ET AL) 27 March 2003 (2003-03-27)
- 2 Document D1, which is considered to represent the most relevant state of the art, discloses modified nucleosides having a 2'-methyl function for the treatment of Flaviviridae infections.  
From this, the subject-matter of claims 1-130 differs in that nucleosides containing a 2'-methyl and a 2'-fluoro function are claimed for the same use.
- 2.1 The subject-matter of claims 1-130 is therefore novel (Article 33(2) PCT)  
The problem to be solved by the present invention may be regarded as:  
the provision of further compounds for the treatment of Flaviviridae infections
- 2.2 The solution to this problem proposed in claims 1-130 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/012472

It is not obvious for the skilled person to substitute the 2'-position with a methyl and a fluoro function, nor is there an incentive in D1 to do so.

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

|                                                                                                                                               |                                                                                   |                                                                       |                  |
|-----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------|------------------|
| Applicant's or agent's file reference<br>60137.2WOU1                                                                                          | <b>FOR FURTHER ACTION</b>                                                         |                                                                       | See item 4 below |
| International application No.<br>PCT/US2004/012472                                                                                            | International filing date ( <i>day/month/year</i> )<br>21 April 2004 (21.04.2004) | Priority date ( <i>day/month/year</i> )<br>30 May 2003 (30.05.2003) ] |                  |
| International Patent Classification (IPC) or national classification and IPC<br>7 C07H 19/06, 19/16, 19/14, A61K 31/7064, 31/7076, A61P 31/12 |                                                                                   |                                                                       |                  |
| Applicant<br>PHARMASSET, INC.                                                                                                                 |                                                                                   |                                                                       |                  |

|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                 |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
|-------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------------|-------------------------------------|------------|----------|-------------------------------------|-------------|--------------------------------------------------------------------------------------------------|--------------------------|------------|----------------------------|-------------------------------------|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|------------|-------------------------|--------------------------|-------------|--------------------------------------------------|--------------------------|--------------|-------------------------------------------------------|
| 1.                                  | This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                 |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| 2.                                  | This REPORT consists of a total of 8 sheets, including this cover sheet.<br><br>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                 |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| 3.                                  | <p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 30%;">Box No. I</td> <td style="width: 60%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> | <input checked="" type="checkbox"/>                                                                                                                             | Box No. I | Basis of the report | <input checked="" type="checkbox"/> | Box No. II | Priority | <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input type="checkbox"/> | Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input type="checkbox"/> | Box No. VI | Certain documents cited | <input type="checkbox"/> | Box No. VII | Certain defects in the international application | <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/> | Box No. I                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Basis of the report                                                                                                                                             |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| <input checked="" type="checkbox"/> | Box No. II                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Priority                                                                                                                                                        |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| <input checked="" type="checkbox"/> | Box No. III                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability                                                                |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| <input type="checkbox"/>            | Box No. IV                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Lack of unity of invention                                                                                                                                      |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| <input checked="" type="checkbox"/> | Box No. V                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| <input type="checkbox"/>            | Box No. VI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Certain documents cited                                                                                                                                         |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| <input type="checkbox"/>            | Box No. VII                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Certain defects in the international application                                                                                                                |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| <input type="checkbox"/>            | Box No. VIII                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Certain observations on the international application                                                                                                           |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |
| 4.                                  | The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis.2).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                 |           |                     |                                     |            |          |                                     |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                          |            |                         |                          |             |                                                  |                          |              |                                                       |

|                                                                                               |                                                                                                                                                                                |
|-----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland | Date of issuance of this report<br><b>01 December 2005 (01.12.2005)</b><br><br>Authorized officer<br><br><div style="text-align: center; font-weight: bold;">Ellen Moyse</div> |
| Facsimile No. +41 22 740 14 35                                                                | Telephone No. +41 22 338 89 75                                                                                                                                                 |

Form PCT/IB/373 (January 2004)

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

REC'D 29 DEC 2004

WIPO

PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/US2004/012472

International filing date (day/month/year)  
21.04.2004

Priority date (day/month/year)  
30.05.2003

International Patent Classification (IPC) or both national classification and IPC  
C07H19/06, C07H19/16, C07H19/14, A61K31/7064, A61K31/7076, A61P31/12

Applicant  
PHARMASSET, INC.

**1. This opinion contains indications relating to the following items:**

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- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
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For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl  
Fax: +31 70 340 - 3016

Authorized Officer

de Nooy, A

Telephone No. +31 70 340-2338



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/012472

---

**Box No. I Basis of the opinion**

---

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/012472

---

**Box No. II Priority**

---

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/012472

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 31-126 (in part)

because:

- ☒ the said international application, or the said claims Nos. 31-126 (in part) relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
  - the written form ☐ has not been furnished
  - ☐ does not comply with the standard
  - the computer readable form ☐ has not been furnished
  - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/012472

---

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

---

1. Statement

|                               |             |               |
|-------------------------------|-------------|---------------|
| Novelty (N)                   | Yes: Claims | 1-130         |
|                               | No: Claims  |               |
| Inventive step (IS)           | Yes: Claims | 1-130         |
|                               | No: Claims  |               |
| Industrial applicability (IA) | Yes: Claims | 1-30, 127-130 |
|                               | No: Claims  |               |

2. Citations and explanations

**see separate sheet**

**Re Item III.**

Claims 31-126 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

For the assessment of the present claims 31-126 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Item V.**

- 1 The following document is referred to in this communication:  
D1 : US 2003/060400 A1 (LACOLLA PAULO ET AL) 27 March 2003 (2003-03-27)
- 2 Document D1, which is considered to represent the most relevant state of the art, discloses modified nucleosides having a 2'-methyl function for the treatment of Flaviviridae infections.  
From this, the subject-matter of claims 1-130 differs in that nucleosides containing a 2'-methyl and a 2'-fluoro function are claimed for the same use.
- 2.1 The subject-matter of claims 1-130 is therefore novel (Article 33(2) PCT)  
The problem to be solved by the present invention may be regarded as:  
the provision of further compounds for the treatment of Flaviviridae infections
- 2.2 The solution to this problem proposed in claims 1-130 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/012472

It is not obvious for the skilled person to substitute the 2'-position with a methyl and a fluoro function, nor is there an incentive in D1 to do so.

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
DAVID G. SCHMALTZ  
MERCHANT & GOULD P.C.  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-0903



## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

|                                                                                   |                                            |                                                                                                           |  |
|-----------------------------------------------------------------------------------|--------------------------------------------|-----------------------------------------------------------------------------------------------------------|--|
| Applicant's or agent's file reference<br>60137.5WOU1                              |                                            | Date of mailing (day/month/year) <b>15 JUN 2006</b><br><b>FOR FURTHER ACTION</b><br>See paragraph 2 below |  |
| International application No.                                                     | International filing date (day/month/year) | Priority date (day/month/year)                                                                            |  |
| PCT/US05/25916                                                                    | 21 July 2005 (21.07.2005)                  | 21 July 2004 (21.07.2004)                                                                                 |  |
| International Patent Classification (IPC) or both national classification and IPC |                                            |                                                                                                           |  |
| IPC(8): Please See Continuation Sheet<br>USPC: 536/4.1,18.6,18.7,22.1,25.3        |                                            |                                                                                                           |  |
| Applicant                                                                         |                                            |                                                                                                           |  |
| PHARMASSET, INC.                                                                  |                                            |                                                                                                           |  |

**1. This opinion contains indications relating to the following items:**

- |                                     |              |                                                                                                                                                                      |
|-------------------------------------|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion                                                                                                                                                 |
| <input type="checkbox"/>            | Box No. II   | Priority                                                                                                                                                             |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability                                                                     |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention                                                                                                                                           |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited                                                                                                                                              |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application                                                                                                                     |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application                                                                                                                |

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

|                                                                                                                                                                                       |                                                                |                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------------|
| Name and mailing address of the ISA/US<br>Mail Stop PCT, Attn: ISA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (571) 273-3201 | Date of completion of this opinion<br>10 May 2006 (10.05.2006) | Authorized officer<br>Patrick T. Lewis<br>Telephone No. 571-272-1600 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------------|

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/25916

**Box No. I Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing  
☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper  
☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.  
☐ filed together with the international application in electronic form.  
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US05/25916

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

|                               |                    |     |
|-------------------------------|--------------------|-----|
| Novelty (N)                   | Claims <u>1-18</u> | YES |
|                               | Claims <u>NONE</u> | NO  |
| Inventive step (IS)           | Claims <u>1-18</u> | YES |
|                               | Claims <u>NONE</u> | NO  |
| Industrial applicability (IA) | Claims <u>1-18</u> | YES |
|                               | Claims <u>NONE</u> | NO  |

2. Citations and explanations:

Claims 1-18 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the instantly claimed 3,5-di-O-protected-2-deoxy-2-fluoro-2-C-methyl-D-ribo- $\gamma$ -lactone.

Claims 1-18 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US05/25916

**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

Continuation of IPC:

C07H 19/00( 2006.01),21/00( 2006.01)

C07H 5/04( 2006.01),5/06( 2006.01);C08B 37/00( 2006.01)

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

|                                                                                                                                  |                                                                                  |                                                                      |                  |
|----------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------|------------------|
| Applicant's or agent's file reference<br>60137.5WOU1                                                                             | <b>FOR FURTHER ACTION</b>                                                        |                                                                      | See item 4 below |
| International application No.<br>PCT/US2005/025916                                                                               | International filing date ( <i>day/month/year</i> )<br>21 July 2005 (21.07.2005) | Priority date ( <i>day/month/year</i> )<br>21 July 2004 (21.07.2004) |                  |
| International Patent Classification (8th edition unless older edition indicated)<br>See relevant information in Form PCT/ISA/237 |                                                                                  |                                                                      |                  |
| Applicant<br>PHARMASSET, INC.                                                                                                    |                                                                                  |                                                                      |                  |

|    |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                 |  |
|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| 1. | This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).                                                                                                               |                                                                                                                                                                 |  |
| 2. | This REPORT consists of a total of 5 sheets, including this cover sheet.<br><br>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead. |                                                                                                                                                                 |  |
| 3. | This report contains indications relating to the following items:                                                                                                                                                                                                                                 |                                                                                                                                                                 |  |
|    | <input checked="" type="checkbox"/> Box No. I                                                                                                                                                                                                                                                     | Basis of the report                                                                                                                                             |  |
|    | <input type="checkbox"/> Box No. II                                                                                                                                                                                                                                                               | Priority                                                                                                                                                        |  |
|    | <input type="checkbox"/> Box No. III                                                                                                                                                                                                                                                              | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability                                                                |  |
|    | <input type="checkbox"/> Box No. IV                                                                                                                                                                                                                                                               | Lack of unity of invention                                                                                                                                      |  |
|    | <input checked="" type="checkbox"/> Box No. V                                                                                                                                                                                                                                                     | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |  |
|    | <input type="checkbox"/> Box No. VI                                                                                                                                                                                                                                                               | Certain documents cited                                                                                                                                         |  |
|    | <input type="checkbox"/> Box No. VII                                                                                                                                                                                                                                                              | Certain defects in the international application                                                                                                                |  |
|    | <input type="checkbox"/> Box No. VIII                                                                                                                                                                                                                                                             | Certain observations on the international application                                                                                                           |  |
| 4. | The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis.2).           |                                                                                                                                                                 |  |

|                                                                                                                                     |                                                                                |
|-------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br><br>Facsimile No. +41 22 338 82 70 | Date of issuance of this report<br>23 January 2007 (23.01.2007)                |
|                                                                                                                                     | Authorized officer<br><br>Athina Nickitas-Etienne<br><br>e-mail: pt04@wipo.int |

Form PCT/IB/373 (January 2004)

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
DAVID G. SCHMALTZ  
MERCHANT & GOULD P.C.  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-0903



## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

|                                                                                                                                                                 |  |                                                                         |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|--|-------------------------------------------------------------------------|--|
| Applicant's or agent's file reference<br>60137.5WOU1                                                                                                            |  | Date of mailing (day/month/year) <b>15 JUN 2006</b>                     |  |
| International application No.<br>PCT/US05/25916                                                                                                                 |  | International filing date (day/month/year)<br>21 July 2005 (21.07.2005) |  |
| International Patent Classification (IPC) or both national classification and IPC<br>IPC(8): Please See Continuation Sheet<br>USPC: 536/4.1,18.6,18.7,22.1,25.3 |  | Priority date (day/month/year)<br>21 July 2004 (21.07.2004)             |  |
| Applicant<br>PHARMASSET, INC.                                                                                                                                   |  |                                                                         |  |

**1. This opinion contains indications relating to the following items:**

- |                                     |              |                                                                                                                                                                      |
|-------------------------------------|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion                                                                                                                                                 |
| <input type="checkbox"/>            | Box No. II   | Priority                                                                                                                                                             |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability                                                                     |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention                                                                                                                                           |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited                                                                                                                                              |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application                                                                                                                     |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application                                                                                                                |

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

|                                                                                                                                                                                       |                                                                |                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------------|
| Name and mailing address of the ISA/US<br>Mail Stop PCT, Attn: ISA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (571) 273-3201 | Date of completion of this opinion<br>10 May 2006 (10.05.2006) | Authorized officer<br>Patrick T. Lewis<br>Telephone No. 571-272-1600 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------------|

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/25916

**Box No. I Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing  
☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper  
☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.  
☐ filed together with the international application in electronic form.  
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US05/25916

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

|                               |                    |     |
|-------------------------------|--------------------|-----|
| Novelty (N)                   | Claims <u>1-18</u> | YES |
|                               | Claims <u>NONE</u> | NO  |
| Inventive step (IS)           | Claims <u>1-18</u> | YES |
|                               | Claims <u>NONE</u> | NO  |
| Industrial applicability (IA) | Claims <u>1-18</u> | YES |
|                               | Claims <u>NONE</u> | NO  |

2. Citations and explanations:

Claims 1-18 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the instantly claimed 3,5-di-O-protected-2-deoxy-2-fluoro-2-C-methyl-D-ribo- $\gamma$ -lactone.

Claims 1-18 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US05/25916

**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

Continuation of IPC:

C07H 19/00( 2006.01),21/00( 2006.01)

C07H 5/04( 2006.01),5/06( 2006.01);C08B 37/00( 2006.01)

Form PCT/ISA/237 (Supplemental Box) (April 2005)

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
STEVEN C. BRUESS  
MERCHANT & GOULD P.C.  
PO BOX 2903  
MINNEAPOLIS, MN 55402-0903

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

|                                                                                                                                                                                           |                                                                              |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Date of mailing<br>(day/month/year) <b>08 MAY 2008</b>                                                                                                                                    |                                                                              |
| <b>FOR FURTHER ACTION</b><br>See paragraph 2 below                                                                                                                                        |                                                                              |
| Applicant's or agent's file reference<br>60137.7WOU1                                                                                                                                      |                                                                              |
| International application No.<br>PCT/US05/32406                                                                                                                                           | International filing date (day/month/year)<br>13 September 2005 (13.09.2005) |
| Priority date (day/month/year)<br>14 September 2004 (14.09.2004)                                                                                                                          |                                                                              |
| International Patent Classification (IPC) or both national classification and IPC<br>IPC(8): A61K 31/70( 2006.01),31/7068( 2006.01),31/7052( 2006.01)<br>USPC: 514/49,43,42;536/28.5,28.4 |                                                                              |
| Applicant<br>PHARMASSET, INC.                                                                                                                                                             |                                                                              |

1. This opinion contains indications relating to the following items:

- |                                     |              |                                                                                                                                                                      |
|-------------------------------------|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion                                                                                                                                                 |
| <input type="checkbox"/>            | Box No. II   | Priority                                                                                                                                                             |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability                                                                     |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention                                                                                                                                           |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited                                                                                                                                              |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application                                                                                                                     |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application                                                                                                                |

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

|                                                                                                                                                                                        |                                                                  |                                                                      |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------------|
| Name and mailing address of the ISA/ US<br>Mail Stop PCT, Attn: ISA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (571) 273-3201 | Date of completion of this opinion<br>28 April 2008 (28.04.2008) | Authorized officer<br>Michael C. Henry<br>Telephone No. 703 308-1235 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------------|

Form PCT/ISA/237 (cover sheet) (April 2007)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/32406

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☐ in electronic form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US05/32406

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

|                               |                                      |     |
|-------------------------------|--------------------------------------|-----|
| Novelty (N)                   | Claims <u>1-31,33-36,38-50,53-83</u> | YES |
|                               | Claims <u>32,37,51,52</u>            | NO  |
| Inventive step (IS)           | Claims <u>1-31,33-36,38-50,53-83</u> | YES |
|                               | Claims <u>32,37,51,52</u>            | NO  |
| Industrial applicability (IA) | Claims <u>1-83</u>                   | YES |
|                               | Claims <u>NONE</u>                   | NO  |

**2. Citations and explanations:**

Claims 1-31, 33-36,38-50,53-83 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the method of preparing or synthesizing the nucleosides or compounds of the given formulas, nor does the prior art teach or fairly suggest the nucleosides or compounds of the given formulas that are set forth in said claims.

Claim 32 lacks novelty under PCT Article 33(2) as being anticipated by HERNANDEZ et al. HERNANDEZ et al. disclose applicant's compound of the general formula, 53C. HERNANDEZ et al compound has a CAS # of 815626-16-5 (see abstract). Claim 37 lacks novelty under PCT Article 33(2) as being anticipated by HERNANDEZ et al. HERNANDEZ et al. disclose applicant's compound of the general formula, 49B. HERNANDEZ et al compound has a CAS # of 815626-16-5 (see abstract).

Claim 51 lacks novelty under PCT Article 33(2) as being anticipated by OISHI et al. OISHI et al. disclose applicant's compound of the general formula, 42B-L wherein OISHI et al.'s compound is represented as compound II (see abstract). Claim 52 lacks novelty under PCT Article 33(2) as being anticipated by OISHI et al. OISHI et al. disclose applicant's compound of the general formula, 42B-L wherein OISHI et al.'s compound is represented as compound II (see abstract).

Claims 1-83 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 8865797                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 18-NOV-2010                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 13:55:02                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

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| Document Number | Document Description | File Name                                   | File Size(Bytes)/<br>Message Digest                | Multi Part /.zip | Pages (if appl.) |
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| 5            | NPL Documents | EP05775359_EPOSup_SearchReportOpinion_091510.pdf | 315962<br>fb88942c066d88e0c70e0c3563d3ec2252d11b65    | no | 10 |
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| 9            | NPL Documents | PCTEP2006069060_WO2007065829_IPER.pdf            | 301528<br>d10212a534449c1dafa5eb2d837c7a0b8c3add0     | no | 7  |
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| 10           | NPL Documents | WO08121634_PCTUS2008058183_WrittenOPN.PDF        | 618352<br>57f865a0b131eaa080d2e0865e3b770dc0d00a      | no | 16 |
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| 11                                                                                                                                                                                                         | NPL Documents | PCTUS2009046619_WO2009152095_092310_ISR.PDF                   | 154199<br>d8d4ee6d0ba3b93b28a9e9f0bae15b18ef30e79ba3 | no | 4  |
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| 14                                                                                                                                                                                                         | NPL Documents | PCTUS2010035641_Invitation_payaddfees_072310.pdf              | 240031<br>9d0a6b1e6c939b5c5a1e6198c25a0d9a117c74469f | no | 7  |
| Warnings:                                                                                                                                                                                                  |               |                                                               |                                                      |    |    |
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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.

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 8866159                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 18-NOV-2010                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 14:17:03                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

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| 1               | Foreign Reference    | WO03104250.pdf | 2015323<br><small>/09062084ded1c2a11197a35838b22a9ff41<br/>07b2</small> | no               | 95               |

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| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                   |                              |                                                       |    |    |
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| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                   |                              |                                                       |    |    |
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| 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Foreign Reference | WO2010075554_p1_to_p74.pdf   | 2110753<br>161d2e6c362bf36d93156c6a0b6d135aa7-bad99   | no | 75 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                   |                              |                                                       |    |    |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                   |                              |                                                       |    |    |
| 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Foreign Reference | WO2010075554_p75_to_p150.pdf | 2121742<br>0b0dd6f58053d1a0e610cc1a68551c016e1c-7d61f | no | 75 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                   |                              |                                                       |    |    |
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| <p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/>If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/>If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/>If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |                   |                              |                                                       |    |    |

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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia et al.          |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| U.S. PATENT DOCUMENTS             |              |            |                                           |       |          |                            |
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| EXAMINER INITIAL                  | DOCUMENT NO. | DATE       | NAME                                      | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                                   |              |            |                                           |       |          |                            |
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|                                   | 20010034440  | 10-25-2001 | Shepard                                   |       |          |                            |
|                                   | 20090137521  | 05-28-2009 | Hamilton<br>(corresponds to WO2009052287) |       |          |                            |
|                                   | 20090233879  | 09-17-2009 | Reddy (corresponds to WO2009115893)       |       |          |                            |
|                                   | 20090280084  | 11-12-2009 | Schinazi<br>(corresponds to WO2009129120) |       |          |                            |
|                                   | 20090306007  | 12-10-2009 | Wagner                                    |       |          |                            |
|                                   | 20100029008  | 02-04-2010 | Stütz (corresponds to WO2006063717)       |       |          |                            |
|                                   | 20100035835  | 02-11-2010 | Narjes (corresponds to WO2008085508)      |       |          |                            |
|                                   | 20100137576  | 06-03-2010 | Stec (corresponds to WO2008048128)        |       |          |                            |
|                                   | 20100173863  | 07-08-2010 | Schinazi                                  |       |          |                            |
|                                   | 20100227801  | 09-09-2010 | Hopkins<br>(corresponds to WO2010080878)  |       |          |                            |
|                                   |              |            |                                           |       |          |                            |
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**23552**

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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia et al.          |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| FOREIGN PATENT DOCUMENTS                                               |                                                                                |            |                                                             |       |          |             |    |
|------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------|-------------------------------------------------------------|-------|----------|-------------|----|
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|                                                                        |                                                                                |            |                                                             |       |          | YES         | NO |
|                                                                        | EP 1828217 A2                                                                  | 09-05-2007 | EP ( <i>corresponds to WO2006063717</i> )                   |       |          |             |    |
|                                                                        | EP 2097430 A1                                                                  | 09-09-2009 | EP ( <i>corresponds to WO2008048128</i> )                   |       |          |             |    |
|                                                                        | EP 2124555 A2                                                                  | 12-02-2009 | EP ( <i>corresponds to WO2008085508</i> )                   |       |          |             |    |
|                                                                        | EP 2207786                                                                     | 07-21-2010 | EP ( <i>corresponds to WO2009052287</i> )                   |       |          |             |    |
|                                                                        | WO 2006063717 A2                                                               | 06-22-2006 | PCT ( <i>corresponds to EP1828217 &amp; US20100029008</i> ) |       |          |             |    |
|                                                                        | WO 2008048128 A1                                                               | 04-24-2008 | PCT ( <i>corresponds to EP2097430 &amp; US20100137576</i> ) |       |          |             |    |
|                                                                        | WO 2008085508                                                                  | 07-17-2008 | PCT ( <i>corresponds to EP2124555 &amp; US20100035835</i> ) |       |          |             |    |
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|                                                                        | WO 2009115893 A2                                                               | 09-24-2009 | PCT ( <i>corresponds to US20090233879</i> )                 |       |          |             |    |
|                                                                        | WO 2009120878 A2                                                               | 10-01-2009 | PCT                                                         |       |          |             |    |
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|                                                                        | WO 2010042834 A1                                                               | 04-15-2010 | PCT                                                         |       |          |             |    |
|                                                                        | WO 2010080878 A1                                                               | 07-15-2010 | PCT ( <i>corresponds to US20100227801</i> )                 |       |          |             |    |
|                                                                        |                                                                                |            |                                                             |       |          |             |    |
| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |                                                                                |            |                                                             |       |          |             |    |
|                                                                        | Gromova et al., Biochem. Biophys. Acta , 1971, 240, 1-11                       |            |                                                             |       |          |             |    |
|                                                                        | Harris et al., Antiviral Chemistry & Chemotherapy, 2002, 12, 293-300           |            |                                                             |       |          |             |    |
|                                                                        | Juodka et al., J. Carbohydrates, Nucleosides, Nucleotides, 1979, 6(4), 333-357 |            |                                                             |       |          |             |    |
|                                                                        | Juodka et al., J. Carbohydrates, Nucleosides, Nucleotides, 1981, 8(1), 19-39   |            |                                                             |       |          |             |    |
|                                                                        | Juodka et al., J. Carbohydrates, Nucleosides, Nucleotides, 1981, 8(6), 519-535 |            |                                                             |       |          |             |    |

**23552**

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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                       | Applicant: Sofia et al.          |                                   |
|                                                                                                                                       | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

|  |  |                                                                                  |
|--|--|----------------------------------------------------------------------------------|
|  |  | Lackey et al., Biochemical Pharmacology, 2001, 61, 179-189                       |
|  |  | McIntee et al., Biorg. & Med. Chem. Lett., 2001, 11, 2803-2805                   |
|  |  | Remy et al., J. Org. Chem., 1962, 27, 2491-2500                                  |
|  |  | Smimov et al., FEBS Letters , 1975, 51(1), 211-214                               |
|  |  | Yuodka et al., translated from Bioorganicheskaya Khimiya, 1976, 2(11), 1513-1519 |

|                                                                                                                                                                                                                                             |                 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| <b>23552</b><br><small>PATENT TRADEMARK OFFICE</small>                                                                                                                                                                                      |                 |
| 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:                              | 9105887                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 23-DEC-2010                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 10:53:12                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description | File Name                                          | File Size(Bytes)/<br>Message Digest               | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|----------------------------------------------------|---------------------------------------------------|------------------|------------------|
| 1               |                      | 12053015_IDS_PTO1449_1222<br>10_60137_0034usu1.pdf | 127371<br>011880260100546dc003898109005d1449-0992 | yes              | 4                |

|              | Multipart Description/PDF files in .zip description  |                          |                                                     |     |     |
|--------------|------------------------------------------------------|--------------------------|-----------------------------------------------------|-----|-----|
|              | Document Description                                 |                          | Start                                               | End |     |
|              | Transmittal Letter                                   |                          | 1                                                   | 1   |     |
|              | Information Disclosure Statement (IDS) Filed (SB/08) |                          | 2                                                   | 4   |     |
| Warnings:    |                                                      |                          |                                                     |     |     |
| Information: |                                                      |                          |                                                     |     |     |
| 2            | Foreign Reference                                    | WO2009120878A2.pdf       | 8616950<br>f09a431af2707921ee8be742c6d134cc31d80    | no  | 194 |
| Warnings:    |                                                      |                          |                                                     |     |     |
| Information: |                                                      |                          |                                                     |     |     |
| 3            | Foreign Reference                                    | WO2010042834A1.pdf       | 3168884<br>355aa94cc04e761848e1807098e611f99913735b | no  | 70  |
| Warnings:    |                                                      |                          |                                                     |     |     |
| Information: |                                                      |                          |                                                     |     |     |
| 4            | NPL Documents                                        | Gromova_1971.PDF         | 500030<br>6a1867cd00f05981d5e9a95a042e6a13ee194a    | no  | 11  |
| Warnings:    |                                                      |                          |                                                     |     |     |
| Information: |                                                      |                          |                                                     |     |     |
| 5            | NPL Documents                                        | Harris_2002.PDF          | 781878<br>f031d570359961ed574c5396937e6a20f339171   | no  | 8   |
| Warnings:    |                                                      |                          |                                                     |     |     |
| Information: |                                                      |                          |                                                     |     |     |
| 6            | NPL Documents                                        | Juodka_1979.PDF          | 704428<br>31aa6f167c2575ced580c7f1a7e0dd2013945b8   | no  | 23  |
| Warnings:    |                                                      |                          |                                                     |     |     |
| Information: |                                                      |                          |                                                     |     |     |
| 7            | NPL Documents                                        | Juodka_1981_19to39.PDF   | 654339<br>f43334b9f7aa096a60f7a099251f43a0e70ff     | no  | 21  |
| Warnings:    |                                                      |                          |                                                     |     |     |
| Information: |                                                      |                          |                                                     |     |     |
| 8            | NPL Documents                                        | Juodka_1981_519to535.PDF | 534520<br>j1c905e110a9067e8210e4f60101b6e7004265c7  | no  | 17  |
| Warnings:    |                                                      |                          |                                                     |     |     |
| Information: |                                                      |                          |                                                     |     |     |

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| 9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | NPL Documents | Lackey_2001.PDF  | 330997<br>d6660082c5b3034dd8da1157c7c91c1d07ee48   | no | 11 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                  |                                                    |    |    |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                  |                                                    |    |    |
| 10                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | NPL Documents | McIntee_2001.PDF | 78735<br>84973e5563ac05c1ad281726e480a411c081588   | no | 3  |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                  |                                                    |    |    |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                  |                                                    |    |    |
| 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | NPL Documents | Remy_1962.PDF    | 1200393<br>f50ad082f01d11675a0f550a431781240c3a099 | no | 10 |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                  |                                                    |    |    |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                  |                                                    |    |    |
| 12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | NPL Documents | Smirnov_1975.PDF | 313900<br>7d446d11f0c0ab0a0b1e726281d71310c576b3   | no | 4  |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                  |                                                    |    |    |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                  |                                                    |    |    |
| 13                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | NPL Documents | Yuodka_1976.PDF  | 495716<br>efdb733c543d1d09866475c95450ad3007d01bad | no | 8  |
| Warnings:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               |                  |                                                    |    |    |
| Information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                  |                                                    |    |    |
| Total Files Size (in bytes):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                  | 17508141                                           |    |    |
| <p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/>If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/>If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/>If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |               |                  |                                                    |    |    |

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|             |                                     |                 |                  |
|-------------|-------------------------------------|-----------------|------------------|
| Applicant:  | Sofia et al.                        | Examiner:       | Lewis, Patrick T |
| Serial No.: | 12/053,015                          | Group Art Unit: | 1623             |
| Filed:      | March 21, 2008                      | Docket No.:     | 60137.0034USU1   |
| 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.

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.

In accordance with 37 C.F.R. § 1.98(a)(2), a copy of each foreign patent and/or a copy of each publication, other than U.S. patents and U.S. patent application publications, listed on the accompanying Form 1449 is enclosed.

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." 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.

If fees are required for consideration of the items listed on the enclosed Form 1449, please charge such fees 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



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## NOTICE OF ALLOWANCE AND FEE(S) DUE

23552 7590 01/05/2011

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

EXAMINER

LEWIS, PATRICK T

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 01/05/2011

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 12/053,015      | 03/21/2008  | MICHAEL JOSEPH SOFIA | 60137.0034USU1      | 3454             |

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          | \$755         | \$300               | \$0                  | \$1055           | 04/05/2011 |

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)

23552 7590 01/05/2011

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

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. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 12/053.015      | 03/21/2008  | MICHAEL JOSEPH SOFIA | 60137.0034USU1      | 3454             |

**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          | \$755         | \$300               | \$0                  | \$1055           | 04/05/2011 |

| EXAMINER         | ART UNIT | CLASS-SUBCLASS |
|------------------|----------|----------------|
| LEWIS, PATRICK T | 1623     | 514-051000     |

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

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 \_\_\_\_\_
- (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. 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.

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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 12/053,015      | 03/21/2008  | MICHAEL JOSEPH SOFIA | 60137.0034USU1      | 3454             |

23552 7590 01/05/2011

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

|          |
|----------|
| EXAMINER |
|----------|

LEWIS, PATRICK T

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

1623

DATE MAILED: 01/05/2011

## 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 291 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 291 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.

|                               |                        |                     |  |
|-------------------------------|------------------------|---------------------|--|
| <b>Notice of Allowability</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                               | 12/053,015             | SOFIA ET AL.        |  |
|                               | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                               | Patrick T. Lewis       | 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 \_\_\_\_.

2. ☒ The allowed claim(s) is/are 13-33.

3. ☐ 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.**

4. ☐ 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.

5. ☐ 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).

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

**Attachment(s)**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)<br>2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)<br>3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br>Paper No./Mail Date <u>01142010; 03182010; 04292010; 04302010;</u><br><u>05042010; 05052010; 05112010; 10282010; 11182010; 12232010</u><br>4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material | 5. <input type="checkbox"/> Notice of Informal Patent Application<br>6. <input type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date ____<br>7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment<br>8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance<br>9. <input type="checkbox"/> Other ____ |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                       |  |
|-------------------------------------------------------|--|
| /Patrick T. Lewis/<br>Primary Examiner, Art Unit 1623 |  |
|-------------------------------------------------------|--|

## DETAILED ACTION

### *Election/Restrictions*

1. Claims 13-15, 19-22, 26-29 and 33 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 16-18, 23-25, and 30-32, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, claims 16-18, 23-25, and 30-32 are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on June 15, 2010 is hereby withdrawn.** In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

***Allowable Subject Matter***

2. The following is an examiner's statement of reasons for allowance: Abraham et al. J. Med. Chem. (1996), Vol. 39, pages 4569-4575 is representative of prior art. Abraham teaches aromatic amino acid phosphoramidites; however, Abraham does not teach nor suggest the instant compound 25.

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

***Contacts***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 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/

|                                                             |                                                |                                                                    |
|-------------------------------------------------------------|------------------------------------------------|--------------------------------------------------------------------|
| <b>Search Notes</b><br><br><b>*1205301</b><br><br><b>5*</b> | <b>Application/Control No.</b><br><br>12053015 | <b>Applicant(s)/Patent Under Reexamination</b><br><br>SOFIA ET AL. |
|                                                             | <b>Examiner</b><br><br>Patrick T Lewis         | <b>Art Unit</b><br><br>1623                                        |

| SEARCHED |          |      |          |
|----------|----------|------|----------|
| Class    | Subclass | Date | Examiner |
|          |          |      |          |

| SEARCH NOTES                                       |            |          |
|----------------------------------------------------|------------|----------|
| Search Notes                                       | Date       | Examiner |
| Inventor, REGISTRY, CAPLUS, MEDLINE (see attached) | 12/17/2010 | /PL/     |

| INTERFERENCE SEARCH |                  |            |          |
|---------------------|------------------|------------|----------|
| Class               | Subclass         | Date       | Examiner |
| 514                 | 43, 49, 50, 51   | 12/17/2010 | /PL/     |
| 536                 | 25.3, 28.1, 28.4 | 12/17/2010 | /PL/     |

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|------------------------------------------------------|------------|-----------------------|-------------------|
| NONE                                                 |            | Total Claims Allowed: |                   |
|                                                      |            | 21                    |                   |
| (Assistant Examiner)                                 | (Date)     |                       |                   |
| /Patrick T Lewis/<br>Primary Examiner, Art Unit 1623 | 12/17/2010 | O.G. Print Claim(s)   | O.G. Print Figure |
| (Primary Examiner)                                   | (Date)     | 1                     | None              |

|                                                                |                                                |                                                                    |
|----------------------------------------------------------------|------------------------------------------------|--------------------------------------------------------------------|
| <b>Index of Claims</b><br><br><b>*1205301</b><br><br><b>5*</b> | <b>Application/Control No.</b><br><br>12053015 | <b>Applicant(s)/Patent Under Reexamination</b><br><br>SOFIA ET AL. |
|                                                                | <b>Examiner</b><br><br>Patrick T Lewis         | <b>Art Unit</b><br><br>1623                                        |

|   |                 |   |                   |   |                     |   |                 |
|---|-----------------|---|-------------------|---|---------------------|---|-----------------|
| ✓ | <b>Rejected</b> | - | <b>Cancelled</b>  | N | <b>Non-Elected</b>  | A | <b>Appeal</b>   |
| = | <b>Allowed</b>  | ÷ | <b>Restricted</b> | I | <b>Interference</b> | O | <b>Objected</b> |

| <input checked="" type="checkbox"/> Claims renumbered in the same order as presented by applicant |          |            |            | <input type="checkbox"/> CPA |  | <input type="checkbox"/> T.D. |  | <input type="checkbox"/> R.1.47 |  |
|---------------------------------------------------------------------------------------------------|----------|------------|------------|------------------------------|--|-------------------------------|--|---------------------------------|--|
| CLAIM                                                                                             |          | DATE       |            |                              |  |                               |  |                                 |  |
| Final                                                                                             | Original | 06/12/2010 | 12/17/2010 |                              |  |                               |  |                                 |  |
|                                                                                                   | 1        | +          | -          |                              |  |                               |  |                                 |  |
|                                                                                                   | 2        | +          | -          |                              |  |                               |  |                                 |  |
|                                                                                                   | 3        | +          | -          |                              |  |                               |  |                                 |  |
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|                                                                                                   | 7        | +          | -          |                              |  |                               |  |                                 |  |
|                                                                                                   | 8        | +          | -          |                              |  |                               |  |                                 |  |
|                                                                                                   | 9        | +          | -          |                              |  |                               |  |                                 |  |
|                                                                                                   | 10       | +          | -          |                              |  |                               |  |                                 |  |
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|                                                                                                   | 33       |            | =          |                              |  |                               |  |                                 |  |

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|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia et al.          |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| U.S. PATENT DOCUMENTS |              |      |      |       |          |                            |
|-----------------------|--------------|------|------|-------|----------|----------------------------|
| EXAMINER INITIAL      | DOCUMENT NO. | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                       |              |      |      |       |          |                            |
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| U.S. PUBLISHED PATENT APPLICATION |              |      |      |       |          |                            |
|-----------------------------------|--------------|------|------|-------|----------|----------------------------|
| EXAMINER INITIAL                  | DOCUMENT NO. | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                                   |              |      |      |       |          |                            |
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| FOREIGN PATENT DOCUMENTS |              |      |         |       |          |             |
|--------------------------|--------------|------|---------|-------|----------|-------------|
|                          | DOCUMENT NO. | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION |
|                          |              |      |         |       |          | YES      NO |
|                          |              |      |         |       |          |             |
|                          |              |      |         |       |          |             |

| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |                                                                                                                                                                                                                                                                                          |
|------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                        | Pogam et al., "No Evidence of R7128 Drug Resistance After Up to 4 Weeks Treatment of GT1, 2 and 3 Hepatitis C Virus Infected Individuals", from 44th Annual Meeting of European Association for the Study of the Liver (EASL), Copenhagen, Denmark Apr 22 - Apr 26, 2009                 |
|                                                                        | Sofia et al., "β-D2'-Deoxy-2'-C-methyluridine Phosphoramidates: Potent and Selective Inhibitors of HCV RNA Replication", Poster # P-259, presented at the 14 <sup>th</sup> International Symposium on Hepatitis C Virus and Related Viruses, Glasgow, Scotland, UK, September 9-13, 2007 |
|                                                                        | Sofia, "β-D-2'-Deoxy-2'-fluoro-2'-C-methyluridine Phosphoramidates: Potent and Selective Inhibitors of HCV RNA Replication", 2nd International Workshop on HCV - Resistance and New Compounds, October 31, 2007                                                                          |
|                                                                        | Sofia et al., "β-D-2'-Deoxy-2'-fluoro-2'-C-methyluridine Phosphoramidates: Potent and Selective Inhibitors of HCV RNA Replication", 2nd International Workshop on HCV", Poster #7, October 31, 2007                                                                                      |
|                                                                        | Sofia et al., "R7128, A Potent and Selective Nucleoside Inhibitor of HCV NS5B Polymerase: An Overview of Clinical Efficacy and Progress Toward Second Generation Inhibitors", From HCV Drug Discovery 2008, Chicago, IL, April 28, 2008                                                  |
|                                                                        | Response filed October 25, 2010 at the EPO for European patent application no. EP08732818.3                                                                                                                                                                                              |

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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
| EXAMINER<br>/Patrick Lewis/ (12/09/2010)                                                                                                                                                                                                    | 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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|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| U.S. PATENT DOCUMENTS |               |            |                                 |       |          |                            |
|-----------------------|---------------|------------|---------------------------------|-------|----------|----------------------------|
| EXAMINER INITIAL      | DOCUMENT NO.  | DATE       | NAME                            | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                       | 5149794       | 09/22/1992 | Yatvin                          |       |          |                            |
|                       | 6777395       | 08/17/2004 | Bhat                            |       |          |                            |
|                       | 7217523       | 05/15/2007 | Wagner                          |       |          |                            |
|                       | 20030120071   | 06/26/2003 | McGuigan                        |       |          |                            |
|                       | 20040266996   | 12/30/2004 | Rabi                            |       |          |                            |
|                       | 20070049754   | 03/1/2007  | Boojamra                        |       |          |                            |
|                       |               |            |                                 |       |          |                            |
|                       |               |            |                                 |       |          |                            |
|                       |               |            |                                 |       |          |                            |
|                       |               |            | <b>FOREIGN PATENT DOCUMENTS</b> |       |          |                            |
|                       | DOCUMENT NO.  | DATE       | COUNTRY                         | CLASS | SUBCLASS | TRANSLATION                |
|                       |               |            |                                 |       |          | YES NO                     |
|                       | WO 03/053989  | 07/03/2003 | PCT                             |       |          |                            |
|                       | WO2005/003147 | 01/13/2005 | PCT                             |       |          |                            |
|                       | WO2006/012078 | 02/02/2006 | PCT                             |       |          |                            |
|                       | WO2006/063149 | 06/15/2006 | PCT                             |       |          |                            |
|                       | WO2006/065335 | 06/22/2006 | PCT                             |       |          |                            |
|                       | WO2008/082601 | 07/10/2008 | PCT                             |       |          |                            |
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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
| EXAMINER<br>/Patrick Lewis/ (12/09/2010)                                                                                                                                                                                                    | DATE CONSIDERED |
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|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |  |                                                                                                                                                                                                                                                                                            |
|------------------------------------------------------------------------|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                        |  | Abraham, et al. "Synthesis, Biological Activity and Decomposition Studies of Amino Acid Phosphomonoester Amides of Acyclovir" Nucleosides, Nucleotides and Nucleic Acids, 1997, 16(10), 2079-2092                                                                                          |
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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
| EXAMINER<br>/Patrick Lewis/ (12/09/2010)                                                                                                                                                                                                    | DATE CONSIDERED |
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\*Substitute Disclosure Statement Form (PTO-1449)  
3764229v1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /P.L./ (12/09/2010)

|                                                                                                                                   |                             |                      |
|-----------------------------------------------------------------------------------------------------------------------------------|-----------------------------|----------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:              | Application Number:  |
|                                                                                                                                   | 60137.0034USU1              | 12/053,015           |
|                                                                                                                                   | Applicant: Sofia            |                      |
|                                                                                                                                   | Filing Date: March 21, 2008 | Group Art Unit: 1623 |

|  |                                                                                                                                                                                                                                                                                                                        |
|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  | Medicinal Chemistry 2000, 43, 2266-2274                                                                                                                                                                                                                                                                                |
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|  | McGuigan, et al. "Synthesis and anti-HIV activity of some novel chain-extended phosphoramidate derivatives of d4T (stavudine): esterase hydrolysis as a rapid predictive test for antiviral potency" Antiviral Chemistry and Chemotherapy, 1998, 9, 109-115                                                            |
|  | McGuigan, et al. "Synthesis and evaluation of some novel phosphoramidate derivatives of 3'-azido-3'-deoxythymidine (AZT) as anti-HIV compounds" Antiviral Chemistry and Chemotherapy, 1990, 1(2), 107-113                                                                                                              |
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|                                                                                                                                       | Applicant: Sofia                 |                                   |
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|                          |               |            |         |       |          | YES           | NO |
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| <div style="border: 1px solid black; padding: 5px; display: inline-block;"> <b>23552</b><br/> <small>PATENT TRADEMARK OFFICE</small> </div>                                                                                                 |                              |
| EXAMINER                                                                                                                                                                                                                                    | /Patrick Lewis/ (12/09/2010) |
| DATE CONSIDERED                                                                                                                                                                                                                             |                              |
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|                                                                                                                                   | Applicant: Sofia                  |                                   |
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| EXAMINER /Patrick Lewis/ (12/09/2010)                                                                                                                                                                                                       | DATE CONSIDERED |
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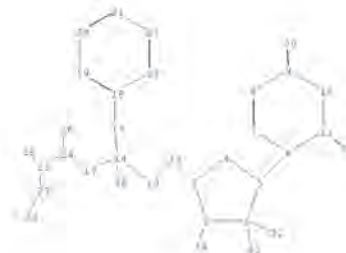
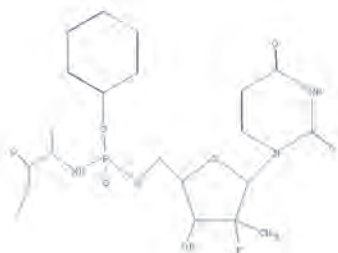
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ring bonds :
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exact/norm bonds :
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normalized bonds :
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Match level :
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END OF SEARCH HISTORY

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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
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|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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|  | <b>DOCUMENT NO.</b> | <b>DATE</b> | <b>COUNTRY</b>                            | <b>CLASS</b> | <b>SUBCLASS</b> | <b>TRANSLATION</b> |           |
|  |                     |             |                                           |              |                 | <b>YES</b>         | <b>NO</b> |
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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
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| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
| EXAMINER<br>/Patrick Lewis/ (12/09/2010)                                                                                                                                                                                                    | DATE CONSIDERED |
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| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                       | Applicant: Sofia                 |                                   |
|                                                                                                                                       | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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|  |  | International Search Report for International Application No. PCT/US2004/012472 (WO2005/003147) mailed December 30, 2004 |
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|  |  | International Search Report for International Application No. PCT/EP2006/069060 (WO2007/065829) mailed January 30, 2007  |
|  |  | International Search Report for International Application No. PCT/US2005/032406 (WO2006/031725) mailed May 8, 2008       |
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| <b>23552</b><br><small>PATENT TRADEMARK OFFICE</small>                                                                                                                                                                                      |                 |
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|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| U.S. PATENT DOCUMENTS |              |            |               |       |          |                            |
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| EXAMINER INITIAL      | DOCUMENT NO. | DATE       | NAME          | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                       | 5192549      | 03-09-1993 | Barenolz      |       |          |                            |
|                       | 5376380      | 12-27-1994 | Kikuchi       |       |          |                            |
|                       | 6060080      | 05-09-2000 | Kikuchi       |       |          |                            |
|                       | 6132763      | 10-17-2000 | Fisher        |       |          |                            |
|                       | 6180134      | 01-30-2001 | Zalipsky      |       |          |                            |
|                       | 6784166      | 08-31-2004 | Devos         |       |          |                            |
|                       | 20030187018  | 10-02-2003 | Llinas-Brunet |       |          |                            |
|                       | 20040229840  | 11-18-2004 | Bhat          |       |          |                            |
|                       | 20050009737  | 01-13-2005 | Clark         |       |          |                            |
|                       | 2005154056   | 07-14-2005 | Yang          |       |          |                            |
|                       | 20050267018  | 12-01-2005 | Blatt         |       |          |                            |
|                       | 20060040890  | 02-23-2006 | Martin        |       |          |                            |
|                       | 20060040927  | 02-23-2006 | Blake         |       |          |                            |
|                       | 20060166964  | 07-27-2006 | Hudyma        |       |          |                            |
|                       | 20060194749  | 08-31-2006 | Keicher       |       |          |                            |
|                       | 20060241064  | 10-26-2006 | Roberts       |       |          |                            |
|                       | 20060276511  | 12-07-2006 | Serrano-Wu    |       |          |                            |
|                       | 20060293306  | 12-28-2006 | Beaulieu      |       |          |                            |
|                       | 20070275947  | 11-29-2007 | Bergstrom     |       |          |                            |
|                       |              |            |               |       |          |                            |

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| <div style="border: 1px solid black; padding: 5px; display: inline-block;"> <b>23552</b><br/> <small>PATENT TRADEMARK OFFICE</small> </div>                                                                                                                |                 |
| EXAMINER<br>/Patrick Lewis/ (12/09/2010)                                                                                                                                                                                                                   | DATE CONSIDERED |
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|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

|  |               |            | FOREIGN PATENT DOCUMENTS |       |          |             |
|--|---------------|------------|--------------------------|-------|----------|-------------|
|  | DOCUMENT NO.  | DATE       | COUNTRY                  | CLASS | SUBCLASS | TRANSLATION |
|  |               |            |                          |       |          | YES NO      |
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|  | WO 2003010141 | 02-06-2003 | PCT                      |       |          |             |
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|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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|  | WO 2006065590 | 06-22-2006 | PCT |  |  |  |
|  | WO 2006093801 | 09-08-2006 | PCT |  |  |  |
|  | WO 2006100310 | 09-28-2006 | PCT |  |  |  |
|  | WO 2006120251 | 11-16-2006 | PCT |  |  |  |
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|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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|                                                                                                                                       | Applicant: Sofia                 |                                   |
|                                                                                                                                       | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

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| <div><b>23552</b><br/><small>PATENT TRADEMARK OFFICE</small></div>                                                                                                                                                                          |                 |
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\*Substitute Disclosure Statement Form (PTO-1449)  
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|             |                                     |                 |                  |
|-------------|-------------------------------------|-----------------|------------------|
| Applicant:  | Sofia, et al.                       | Examiner:       | Lewis, Patrick T |
| Serial No.: | 12/053,015                          | Group Art Unit: | 1623             |
| Filed:      | March 21, 2008                      | Docket No.:     | 60137.0034USUI   |
| Title:      | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                 |                  |

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INFORMATION DISCLOSURE STATEMENT

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 related patents and patent applications, the subject matter of which is summarized below. Applicants also request that the Examiner consider the previously issued Office Actions for these patents and patent applications. Copies of the issued or pending claims of these patents and patent applications and their respective office actions to date are attached to this document. Furthermore, each of these items are listed on the attached modified PTO-1449 form. 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.

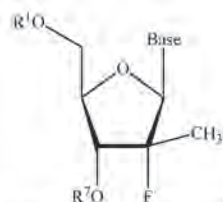
- (1) U.S. Patent No. 7,429,572 ("the '572 patent") issued on September 30, 2008, which issued from U.S. Application No. 10/828,753, filed April 21, 2004 and published as US 2005/0009737 on January 13, 2005.

Claim 1 of the '572 patent is directed to a compound or its pharmaceutically acceptable salt having the following structure:

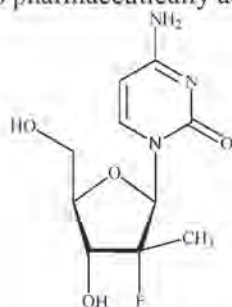
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/Patrick Lewis/ (12/09/2010)

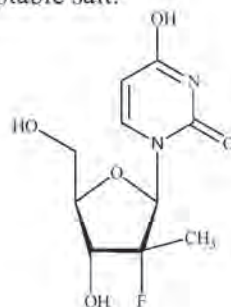
U.S. Application No. 12/053,015  
Date submitted: March 18, 2010



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



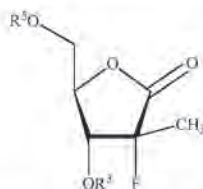
Claim 6



Claim 14

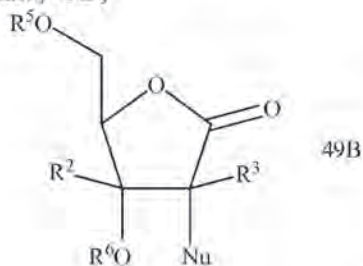
- (2) U.S. Patent No. 7,601,820 ("the '820 patent") issued on October 13, 2009 from U.S. Patent Application No. 11/353,597 ("the '597 application"), filed February 13, 2006 and published as US 2006/0199783 on September 7, 2006.

Claim 1 of the '820 patent is directed to a compound of the following formula:



- (3) U.S. Application No. 11/225,425 ("the '425 application"), filed September 13, 2005, published as US 2006/0122146 on June 8, 2006.

Claim 37 of the '425 application is directed to a compound of the following general formula, 49B,



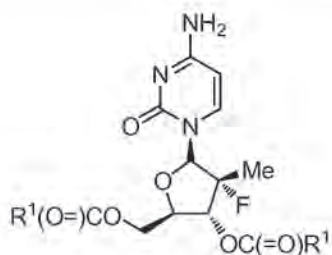
49B

U.S. Application No. 12/053,015  
Date submitted: March 18, 2010

The remaining independent claims of the '425 application, claims 84 and 85, are presently withdrawn from consideration. As noted above, a copy of presently pending claims of the '425 application is attached herewith.

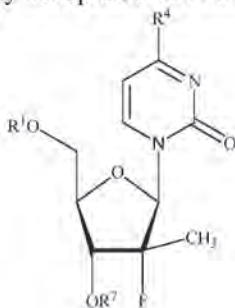
- (4) U.S. Application No. 11/635,898 ("the '898 application"), filed December 8, 2006, published as US 2007/0197463 on August 23, 2007.

Claim 1 of the '898 application is directed to the following compound and acid addition salts thereof, while claim 16 is directed to a process for preparing the same.



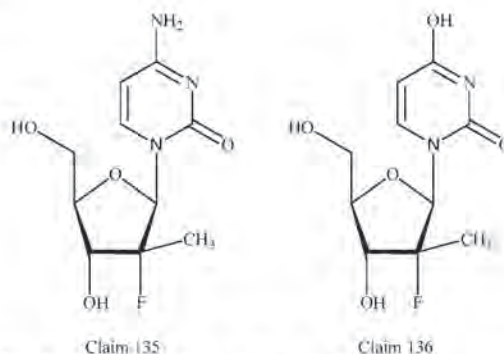
- (5) U.S. Application No. 11/854,218 ("the '218 application"), filed September 12, 2007, published as US 2008/0070861 on March 20, 2008;

Claim 130 of the '218 application is directed to 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 compound ( $\beta$ -D or  $\beta$ -L) or its pharmaceutically acceptable salt having the following structure.



Claims 135 and 136 of the '218 application are directed to 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 compound ( $\beta$ -D) or its pharmaceutically acceptable salt having the following respective structures.

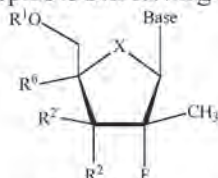
U.S. Application No. 12/053,015  
Date submitted: March 18, 2010



Claims 137, 142, and 143 are also method of treatment claims. As noted above, a copy of the presently pending claims are attached herewith.

- (6) U.S. Application No. 12/142,536 ("the '536 application"), filed June 19, 2008, published as US 2009/0004135 on January 1, 2009;

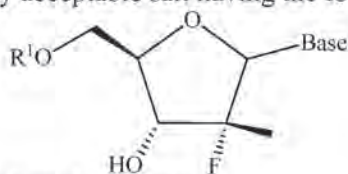
Claim 130 of the '536 application is directed to a compound ( $\beta$ -d or  $\beta$ -l) or its pharmaceutically acceptable salt having the following structure:



where the base is a purine base. The '536 application contains other independent claims, as seen by a copy of the pending claims attached herewith.

- (7) U.S. Application No. 12/142,554 ("the '554 application"), filed June 19, 2008, published as US2008/0253995 on October 16, 2008.

Claim 201 of the '554 application is directed to a compound ( $\beta$ -d or  $\beta$ -l) or its pharmaceutically acceptable salt having the following structure;

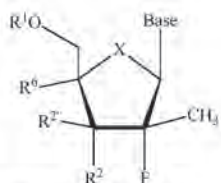


where the base is a pyrrolopyrimidine base.

- (8) U.S. Application No. 12/240,342 ("the '342 application"), filed on September 29, 2008, published as 2009/0036666 on February 5, 2009.

Claim 130 of the '342 application is directed to a compound

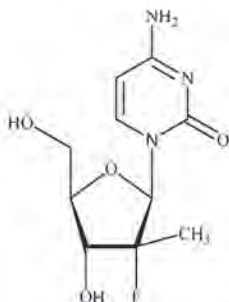
U.S Application No. 12/053,015  
Date submitted: March 18, 2010



where base is a purine or a pyrimidine.

- (9) U.S. Patent Application No. 12/553,483 ("the '483 application"), filed September 9, 2009, which is a continuation of U.S Application No. the '597 application (No. 1 above), published as US 2010/0048917 on February 25, 2010.

Claim 20 of the '483 application is directed to a process for preparing the following compound:



Applicants also ask that the Examiner consider the claims of U.S. Patent Application Nos. 12/479,075; 12/645,710; 12/645,765; and 12/645,821. As these applications are not yet open to the public (37 CFR 1.11), Applicants have not submitted the claims herewith.

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: March 18, 2010

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

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(FILE 'HOME' ENTERED AT 22:49:36 ON 09 DEC 2010)

FILE 'REGISTRY' ENTERED AT 22:49:51 ON 09 DEC 2010
L1      STRUCTURE UPLOADED
L2      23 S L1 SSS SAM
L3      303 S L1 SSS FULL

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L4      840 S L3

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L5      STRUCTURE UPLOADED
L6      0 S L5 SSS SAM
L7      1 S L5 SSS FULL

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L8      1 S L7

FILE 'REGISTRY' ENTERED AT 22:57:51 ON 09 DEC 2010
L9      STRUCTURE UPLOADED
L10     0 S L9 SSS SAM
L11     1 S L9 SSS FULL

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L12     1 S L11

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L15     8 S L13 SSS FULL

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L20     832 S L19

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FILE 'CAPLUS, MEDLINE' ENTERED AT 23:52:32 ON 09 DEC 2010

FILE 'STINGUIDE' ENTERED AT 23:52:48 ON 09 DEC 2010

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|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia et al.          |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| U.S. PATENT DOCUMENTS |              |            |                                 |       |          |                            |
|-----------------------|--------------|------------|---------------------------------|-------|----------|----------------------------|
| EXAMINER INITIAL      | DOCUMENT NO. | DATE       | NAME                            | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                       | 6348587      | 02-19-2002 | Schinazi                        |       |          |                            |
|                       | 6455513      | 09-24-2002 | McGuigan                        |       |          |                            |
|                       | 6911424      | 06-28-2005 | Schinazi                        |       |          |                            |
|                       | 7018989      | 03-28-2006 | McGuigan                        |       |          |                            |
|                       | 7105499      | 09-12-2006 | Carroll                         |       |          |                            |
|                       | 7307065      | 12-11-2007 | Schinazi                        |       |          |                            |
|                       | 7429572      | 09-30-2008 | Clark                           |       |          |                            |
|                       | 20050009737  | 01-13-2005 | Clark                           |       |          |                            |
|                       | 20060142238  | 06-29-2006 | McGuigan                        |       |          |                            |
|                       | 20070042988  | 02-22-2007 | Klumpp                          |       |          |                            |
|                       | 20070087960  | 04-19-2007 | Storer                          |       |          |                            |
|                       | 20070197463  | 08-23-2007 | Chun                            |       |          |                            |
|                       | 20070265222  | 11-15-2007 | MacCoss                         |       |          |                            |
|                       | 20070275912  | 11-29-2007 | Bhat                            |       |          |                            |
|                       |              |            |                                 |       |          |                            |
|                       |              |            |                                 |       |          |                            |
|                       |              |            | <b>FOREIGN PATENT DOCUMENTS</b> |       |          |                            |
|                       | DOCUMENT NO. | DATE       | COUNTRY                         | CLASS | SUBCLASS | TRANSLATION                |
|                       |              |            |                                 |       |          | YES NO                     |
|                       | WO2005012327 | 02-10-2005 | PCT                             |       |          |                            |
|                       | WO2006063149 | 06-15-2006 | PCT                             |       |          |                            |
|                       | WO2006121820 | 11-16-2006 | PCT                             |       |          |                            |
|                       | WO2007095269 | 08-23-2007 | PCT                             |       |          |                            |
|                       | WO2008062206 | 05-29-2008 | PCT                             |       |          |                            |
|                       | WO2008079206 | 07-03-2008 | PCT                             |       |          |                            |

**23552**

PATENT TRADEMARK OFFICE

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|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-----------------|
| EXAMINER                                                                                                                                                                                                                                    | /Patrick Lewis/ (12/09/2010) | 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. |                              |                 |

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /P.L./ (12/09/2010)

|                                                                                                                                   |                                  |                                   |
|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia et al.          |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

|  |              |            |     |  |  |  |  |
|--|--------------|------------|-----|--|--|--|--|
|  | WO2008142055 | 11-27-2008 | PCT |  |  |  |  |
|  |              |            |     |  |  |  |  |

**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

|  |  |                                                                                      |
|--|--|--------------------------------------------------------------------------------------|
|  |  | Aquaro, et al. Antimicrobial Agents and Chemotherapy, 2000, 1, 173-177               |
|  |  | Chapman, et al. Nucleotides, Nucleosides and Nucleic Acids, 2001, 20(4-7), 1085-1090 |
|  |  | Chapman, et al. Nucleotides, Nucleosides and Nucleic Acids, 2001, 20(4-7), 621-628   |
|  |  | 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             |
|  |  | McGuigan, et al. Antiviral Chemistry and Chemotherapy 1998, 9, 473-479               |
|  |  | Murakami et al. Antimicrobial Agents and Chemotherapy (Feb. 2008), 52 (2), 458-464   |
|  |  | Murakami, et al. Antiviral Chemistry & Chemotherapy, 2007, 51(2), 503-509            |
|  |  | Ray, et al. Antimicrobial Agents and Chemotherapy, 2008, 52(2), 648-654              |
|  |  | Stuyver, L.J. et al. Antiviral Chemistry & Chemotherapy, 2004, 48(2), 651-654        |
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**23552**

PATENT/TRADEMARK OFFICE

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|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| EXAMINER /Patrick Lewis/ (12/09/2010)                                                                                                                                                                                                       | 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. |                 |

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /P.L./ (12/09/2010)

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|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia et al.          |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| U.S. PATENT DOCUMENTS |              |            |       |       |          |                            |
|-----------------------|--------------|------------|-------|-------|----------|----------------------------|
| EXAMINER INITIAL      | DOCUMENT NO. | DATE       | NAME  | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                       | 7429572      | 09-30-2008 | Clark | /     | /        |                            |
|                       | 7601820      | 10-13-2009 | Wang  | /     | /        |                            |
|                       |              |            |       |       |          |                            |
|                       |              |            |       |       |          |                            |

| FOREIGN PATENT DOCUMENTS |              |      |         |       |          |             |
|--------------------------|--------------|------|---------|-------|----------|-------------|
|                          | DOCUMENT NO. | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION |
|                          |              |      |         |       |          | YES NO      |
|                          |              |      |         |       |          |             |

| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |                                                                       |
|------------------------------------------------------------------------|-----------------------------------------------------------------------|
|                                                                        | U.S. application no. 10/828,753 Non-Final Rejection mailed 03-30-2007 |
|                                                                        | U.S. application no. 10/828,753 Final Rejection mailed 02-26-2008     |
|                                                                        | U.S. application no. 11/225,425 Non-Final Rejection mailed 11-13-2008 |
|                                                                        | U.S. application no. 11/225,425 Non-Final Rejection mailed 07-07-2009 |
|                                                                        | U.S. application no. 11/225,425 pending claims filed 10-02-2009       |
|                                                                        | U.S. application no. 11/225,425 Final Rejection mailed 02-18-2010     |
|                                                                        | U.S. application no. 11/353,597 Non-Final Rejection mailed 10-02-2007 |
|                                                                        | U.S. application no. 11/353,597 Non-Final Rejection mailed 07-17-2008 |
|                                                                        | U.S. application no. 11/353,597 Final Rejection mailed 12-02-2008     |
|                                                                        | U.S. application no. 11/635,898 Non-Final Rejection mailed 07-28-2009 |
|                                                                        | U.S. application no. 11/635,898 pending claims filed 12-24-2009       |
|                                                                        | U.S. application no. 11/854,218 pending claims filed 09-12-2007       |
|                                                                        | U.S. application no. 11/854,218 Non-Final Rejection mailed 10-01-2009 |
|                                                                        | U.S. application no. 12/142,536 pending claims filed 06-19-2008       |
|                                                                        | U.S. application no. 12/142,536 Non-Final Rejection mailed 10-02-2009 |
|                                                                        | U.S. application no. 12/142,554 Non-Final Rejection mailed 10-01-2009 |

**23552**

PATENT TRADEMARK OFFICE

|                                       |                 |
|---------------------------------------|-----------------|
| EXAMINER /Patrick Lewis/ (12/09/2010) | 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.

\*Substitute Disclosure Statement Form (PTO-1449)  
4343031v1

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /P.L./ (12/09/2010)

|                                                                                                                                   |                                  |                                   |
|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia et al.          |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

|  |                                                                       |
|--|-----------------------------------------------------------------------|
|  | U.S. application no. 12/142,554 pending claims filed 12-17-2009       |
|  | U.S. application no. 12/240,342 pending claims filed 09-29-2008       |
|  | U.S. application no. 12/240,342 Non-Final Rejection mailed 10-01-2009 |
|  | U.S. application no. 12/479,075 filed 06-05-2009                      |
|  | U.S. application no. 12/553,483 Non-Final Rejection mailed 12-17-2009 |
|  | U.S. application no. 12/553,483 pending claims filed 02-22-2010       |
|  | U.S. application no. 12/645,710 filed 12-23-2009                      |
|  | U.S. application no. 12/645,765 filed 12-23-2009                      |
|  | U.S. application no. 12/645,821 filed 12-23-2009                      |

**23552**

PATENT TRADEMARK OFFICE

EXAMINER /Patrick Lewis/ (12/09/2010)

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.

\*Substitute Disclosure Statement Form (PTO-1449)  
 4343031v1

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /P.L./ (12/09/2010)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|               |                                     |                   |                   |
|---------------|-------------------------------------|-------------------|-------------------|
| Applicant:    | Michael J. Sofia et al.             | Examiner:         | LEWIS, PATRICK T. |
| Serial No.:   | 12/053,015                          | Group Art Unit:   | 1623              |
| Filed:        | March 21, 2008                      | Docket No.:       | 60137.0034USU1    |
| Customer No.: | 23552                               | Confirmation No.: | 3454              |
| Title:        | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                   |                   |

---

RULE 312 AMENDMENT

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

Dear Sir:

Further to the Notice Allowability dated January 5, 2011, Applicants request that the Examiner act on the concurrently filed Rule 48(b) – Request to Correct Inventorship before the allowed application issues as a U.S. patent and enter the present amendment prior to issuance of the claims.

**Amendments to the Claims** begin on page 2 of this paper.

**Remarks** begin on page 7 of this paper.

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

Claims 1-12 (Canceled).

Claim 13 (Previously Presented): (S)-2-{[(2R,3R,4R,5R)-5-(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.

Claim 14 (Previously Presented): A composition comprising the compound or a stereoisomer thereof as claimed in claim 13 and a pharmaceutically acceptable medium.

Claim 15 (Previously Presented): A composition for treating a hepatitis C virus, which comprises an effective amount of the compound or a stereoisomer thereof as claimed in claim 13 and a pharmaceutically acceptable medium.

Claim 16 (Previously Presented): A method of treating a subject infected by a virus, which comprises:

administering to the subject an effective amount of the compound or a stereoisomer thereof as claimed in claim 13;

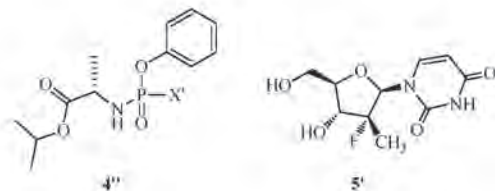
wherein the virus is selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus.

Claim 17 (Previously Presented): A method of treating a hepatitis C virus infection in a subject in need thereof, which comprises:

administering to the subject an effective amount of the compound or a stereoisomer thereof as claimed in claim 13,

Claim 18 (Previously Presented): A process for preparing the compound or a stereoisomer thereof as claimed in claim 13, said process comprising:

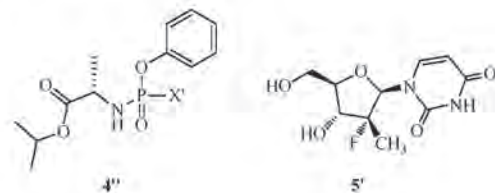
reacting a compound **4''** with a nucleoside analog **5'**



wherein X' is a leaving group.

Claim 19 (Previously Presented): A product comprising the compound or a stereoisomer thereof as claimed in claim 13 obtained by a process comprising:

reacting a compound **4''** with a nucleoside analog **5'**



wherein X' is a leaving group.

Claim 20 (Previously Presented): (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.

Claim 21 (Previously Presented): A composition comprising the compound as claimed in claim 20 and a pharmaceutically acceptable medium.

Claim 22 (Previously Presented): A composition for treating a hepatitis C virus, which comprises an effective amount of the compound as claimed in claim 20 and a pharmaceutically acceptable medium.

Claim 23 (Previously Presented): A method of treating a subject infected by a virus, which comprises:

administering to the subject an effective amount of the compound as claimed in claim 20;

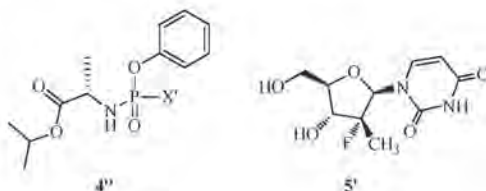
wherein the virus is selected from among hepatitis C virus, West Nile virus, a yellow fever virus, a dengue virus, a rhinovirus, a polio virus, a hepatitis A virus, a bovine viral diarrhea virus, and a Japanese encephalitis virus.

Claim 24 (Previously Presented): A method of treating a 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 claim 20.

Claim 25 (Previously Presented): A process for preparing the compound as claimed in claim 20, said process comprising:

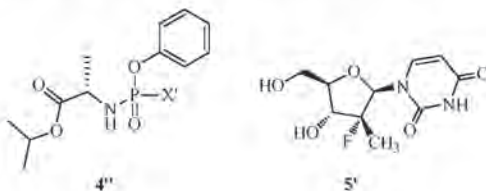
reacting a compound 4'' with a nucleoside analog 5'



wherein X' is a leaving group.

Claim 26 (Previously Presented): A product comprising the compound as claimed in claim 20 obtained by a process comprising:

reacting a compound 4'' with a nucleoside analog 5'



wherein X' is a leaving group.

Application No. 12/053,015  
Further to the Notice Allowability dated January 5, 2011

Claims 27-33 (Canceled).

Application No. 12/053,015  
Further to the Notice Allowability dated January 5, 2011

**REMARKS**

Applicants thank the Examiner for allowing claims 13-33. The present amendment serves to cancel allowed claims 27-33 without prejudice or disclaimer. Applicants reserve the right to claim the subject matter of claims 27-33 in a continuing application. It is believed that entry of the amendment raises no new issues for consideration by the Examiner. Accordingly, it is respectfully requested that the Examiner enter the amendment and allow claims 13-26 to pass to issue.

Applicants note that the allowed claims are related to certain claims presented in US 12/783,680, filed on May 20, 2010, which published as US 2010/0298257 on November 25, 2010. The subject matter of US 12/783,680 has not been examined. The independent claims of this patent application are attached as **Exhibit A** to this document. US 12/783,680 corresponds to PCT/US2010/035641, which published as WO 2010/135569 on November 25, 2010. The Written Opinion and International Search Report were cited in this application on November 18, 2010, and considered by the Examiner on December 9, 2010.

Applicants also request that the Examiner grant the concurrently filed Rule 48(b) petition.

No additional fee is believed to be due; however, the Director is hereby authorized to charge any fees that may be required or credit any overpayment to Deposit Account 13-2725.



Respectfully submitted,  
MERCHANT & GOULD P.C.  
P.O. Box 2903  
Minneapolis, Minnesota 55402-0903  
(404) 954-5061

A handwritten signature in black ink, appearing to read "Daniel R. Evans".

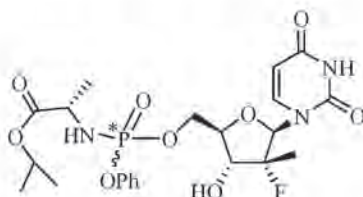
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Daniel R. Evans, Ph.D.  
Registration No. 55,868

Date: April 1, 2011

**EXHIBIT A – Pending Independent Claims of US 12/783,680**

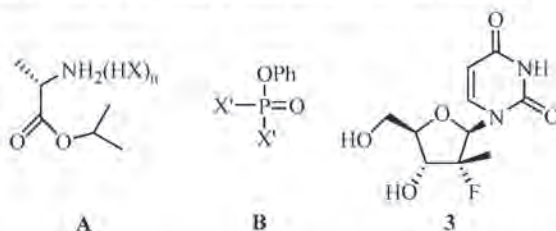
1. A process for preparing compound represented by formula **4**:



**4**

wherein P\* represents a chiral phosphorus atom, which comprises:

- a) reacting an isopropyl-alanate, **A**, a di-X'-phenylphosphate, **B**, 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a base to obtain a first mixture comprising **4**;



**A**

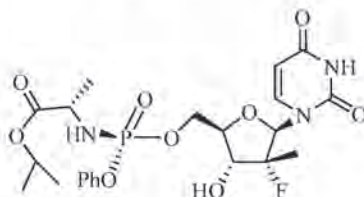
**B**

**3**

wherein X is a conjugate base of an acid, n is 0 or 1, and X' is a halogen

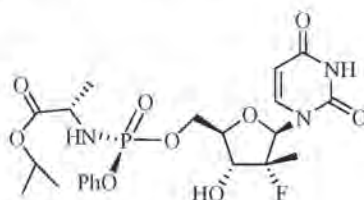
- b) reacting the first mixture with a protecting compound to obtain a second mixture comprising **4**; and  
c) optionally subjecting the second mixture to crystallization, chromatography, or extraction in order to obtain **4**.

13. A compound represented by the formula **R<sub>p</sub>-4**



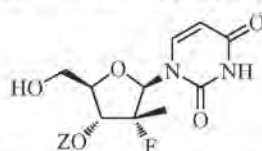
**R<sub>p</sub>-4**

35. A compound represented by the formula **S<sub>p</sub>-4**



Sp-4

70. A compound selected from among **3a**, **3b**, **3c**, and **3d**



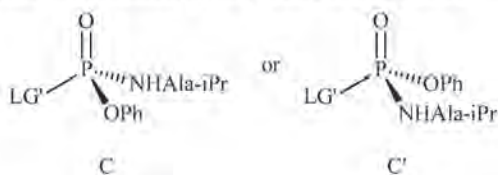
**3a**: Z = -C(O)CH<sub>2</sub>CH<sub>2</sub>C(O)CH<sub>3</sub>

**3b**: Z = -C(O)OCH<sub>2</sub>Ph

**3c**: Z = -Si(Me)<sub>2</sub><sup>t</sup>Bu

**3d**: Z = -Si(<sup>t</sup>Pr)<sub>2</sub>OSi(<sup>t</sup>Pr)<sub>2</sub>OH

71. A compound represented by the following structures



where LG' is a leaving group.

76. [(S)-2-[(S)-(4-nitro-phenoxy)-phenoxy-phosphorylamino] propionic acid isopropyl ester (**8**, Sp-isomer).

77. Crystalline [(S)-2-[(S)-(4-nitro-phenoxy)-phenoxy-phosphorylamino] propionic acid isopropyl ester (**8**, Sp-isomer).

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|               |                                     |                   |                   |
|---------------|-------------------------------------|-------------------|-------------------|
| Applicant:    | Michael J. Sofia et al.             | Examiner:         | LEWIS, PATRICK T. |
| Serial No.:   | 12/053,015                          | Group Art Unit:   | 1623              |
| Filed:        | March 21, 2008                      | Docket No.:       | 60137.0034USU1    |
| Customer No.: | 23552                               | Confirmation No.: | 3454              |
| Title:        | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                   |                   |

RULE 48(b) – REQUEST FOR CORRECTION OF INVENTORSHIP

Mail Stop Amendment  
COMMISSIONER FOR PATENTS  
P.O. BOX 1450  
ALEXANDRIA, VIRGINIA 22313-1450

Dear Examiner Lewis:

Applicants request that Dhanapalan Nagarathnam be deleted as an inventor from the above-identified application.

Michael Joseph Sofia, Jinfa Du, Peiyuan Wang, and Dhanapalan Nagarathnam are the named inventors of the present application. The present application contains disclosed subject matter which is attributable to Messrs. Sofia, Du, Wang, and Nagarathnam; but it is noted that Messrs. Sofia, Wang, and Du are the inventors of allowed claims 13-33.

Applicants informed Applicants' representative of this fact prior to October 28, 2010, but Applicants' representative inadvertently failed to file the necessary Rule 48(b) request. Accordingly, Applicants' representative kindly requests that the Office GRANT Applicants' request to delete Dhanapalan Nagarathnam as an inventor.

Applicants have submitted the necessary Rule 17(i) processing fee of \$130. No additional fee is believed to be due; however, the Director is hereby authorized to charge any fees that may be required or credit any overpayment to Deposit Account 13-2725.



Respectfully submitted,  
MERCHANT & GOULD P.C.  
P.O. Box 2903  
Minneapolis, Minnesota 55402-0903  
(404) 954-5061

/Daniel R. Evans/  
Daniel R. Evans, Ph.D.  
Registration No. 55,868

Date: April 1, 2011

| Electronic Patent Application Fee Transmittal |          |                                     |        |                      |
|-----------------------------------------------|----------|-------------------------------------|--------|----------------------|
| Application Number:                           |          | 12053015                            |        |                      |
| Filing Date:                                  |          | 21-Mar-2008                         |        |                      |
| Title of Invention:                           |          | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |        |                      |
| First Named Inventor/Applicant Name:          |          | MICHAEL JOSEPH SOFIA                |        |                      |
| Filer:                                        |          | Daniel R. Evans/AMY ALBA            |        |                      |
| Attorney Docket Number:                       |          | 60137.0034USU1                      |        |                      |
| Filed as Small 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:                            |          |                                     |        |                      |

| Description                             | Fee Code | Quantity | Amount | Sub-Total in USD(\$) |
|-----------------------------------------|----------|----------|--------|----------------------|
| <b>Miscellaneous:</b>                   |          |          |        |                      |
| Processing Fee, except for Provis. apps | 1808     | 1        | 130    | 130                  |
| <b>Total in USD (\$)</b>                |          |          |        | <b>130</b>           |

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 9792905                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 01-APR-2011                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 15:38:32                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                                                                                                                                                                                                                                                                                                                                                     |                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| Submitted with Payment                                                                                                                                                                                                                                                                                                                              | yes             |
| Payment Type                                                                                                                                                                                                                                                                                                                                        | Credit Card     |
| Payment was successfully received in RAM                                                                                                                                                                                                                                                                                                            | \$ 130          |
| RAM confirmation Number                                                                                                                                                                                                                                                                                                                             | 1973            |
| Deposit Account                                                                                                                                                                                                                                                                                                                                     | 132725          |
| Authorized User                                                                                                                                                                                                                                                                                                                                     | EVANS,DANIEL R. |
| <p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)</p> |                 |

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               |                      | 12053915_Rule312Amendmen<br>t_60137_0034usu1.pdf | 139553<br>8251b77b7d54e19dd5eb98da06e70net4b<br>ce/e4 | yes              | 8                |

## Multipart Description/PDF files in .zip description

| Document Description                             | Start | End |
|--------------------------------------------------|-------|-----|
| Amendment after Notice of Allowance (Rule 312)   | 1     | 1   |
| Claims                                           | 2     | 5   |
| Applicant Arguments/Remarks Made in an Amendment | 6     | 8   |

## Warnings:

## Information:

|   |                                               |                                                                       |                                                       |    |   |
|---|-----------------------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------|----|---|
| 2 | Request under Rule 48 correcting inventorship | 12053015_Rule48b_ReqCorrect<br>ionInventorship_60137_0034us<br>u1.pdf | 60001<br>0b03b030f6fbb70c29e99f9810921695528<br>bc216 | no | 1 |
|---|-----------------------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------|----|---|

## Warnings:

## Information:

|   |                         |              |                                                       |    |   |
|---|-------------------------|--------------|-------------------------------------------------------|----|---|
| 3 | Fee Worksheet (PTO-875) | fee-info.pdf | 30272<br>b1d4d10c23e6f92617a4b03458cfa191a4c<br>710eb | no | 2 |
|---|-------------------------|--------------|-------------------------------------------------------|----|---|

## Warnings:

## Information:

Total Files Size (in bytes): 229826

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)

23552 7590 01/05/2011

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

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. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 12/053.015      | 03/21/2008  | MICHAEL JOSEPH SOFIA | 60137.0034USU1      | 3454             |

**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          | \$755         | \$300               | \$0                  | \$1055           | 04/05/2011 |

| EXAMINER         | ART UNIT | CLASS-SUBCLASS |
|------------------|----------|----------------|
| LEWIS, PATRICK T | 1623     | 514-051000     |

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

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

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

1 Merchant & Gould, PC

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)

**Pharmasset, Inc.**

**Princeton, NJ**

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 13-2725 (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 /Daniel R. Evans/

Date April 5, 2011

Typed or printed name Daniel R. Evans

Registration No. 55868

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.

| Electronic Patent Application Fee Transmittal |          |                                     |        |                      |
|-----------------------------------------------|----------|-------------------------------------|--------|----------------------|
| Application Number:                           |          | 12053015                            |        |                      |
| Filing Date:                                  |          | 21-Mar-2008                         |        |                      |
| Title of Invention:                           |          | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |        |                      |
| First Named Inventor/Applicant Name:          |          | MICHAEL JOSEPH SOFIA                |        |                      |
| Filer:                                        |          | Daniel R. Evans/AMY ALBA            |        |                      |
| Attorney Docket Number:                       |          | 60137.0034USU1                      |        |                      |
| Filed as Small Entity                         |          |                                     |        |                      |
| Utility under 35 USC 111(a) Filing Fees       |          |                                     |        |                      |
| Description                                   | Fee Code | Quantity                            | Amount | Sub-Total in USD(\$) |
| Basic Filing:                                 |          |                                     |        |                      |
| Pages:                                        |          |                                     |        |                      |
| Claims:                                       |          |                                     |        |                      |
| Miscellaneous-Filing:                         |          |                                     |        |                      |
| Publ. Fee- early, voluntary, or normal        | 1504     | 1                                   | 300    | 300                  |
| Petition:                                     |          |                                     |        |                      |
| Patent-Appeals-and-Interference:              |          |                                     |        |                      |
| Post-Allowance-and-Post-Issuance:             |          |                                     |        |                      |
| Utility Appl issue fee                        | 2501     | 1                                   | 755    | 755                  |

| Description        | Fee Code | Quantity | Amount | Sub-Total in USD(\$) |
|--------------------|----------|----------|--------|----------------------|
| Extension-of-Time: |          |          |        |                      |
| Miscellaneous:     |          |          |        |                      |
| Total in USD (\$)  |          |          |        | 1055                 |

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 9813146                             |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 05-APR-2011                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 15:31:43                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                                                                                                                                                                                                                                                                                                                   |                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| Submitted with Payment                                                                                                                                                                                                                                                                                            | yes             |
| Payment Type                                                                                                                                                                                                                                                                                                      | Credit Card     |
| Payment was successfully received in RAM                                                                                                                                                                                                                                                                          | \$ 1055         |
| RAM confirmation Number                                                                                                                                                                                                                                                                                           | 2000            |
| Deposit Account                                                                                                                                                                                                                                                                                                   | 132725          |
| Authorized User                                                                                                                                                                                                                                                                                                   | EVANS,DANIEL R. |
| <p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)</p> |                 |

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) | 12053015_IssueFeeTransmittal_040511_60137_0034usu1.pdf | 510848<br>01a00c0f0ee480557110050a50a57006e20d605 | no               | 1                |

### Warnings:

### Information:

|   |                         |              |                                              |    |   |
|---|-------------------------|--------------|----------------------------------------------|----|---|
| 2 | Fee Worksheet (PTO-875) | fee-info.pdf | 31705<br>590604130c3b0b0e6d0a097246085019162 | no | 2 |
|---|-------------------------|--------------|----------------------------------------------|----|---|

### Warnings:

### Information:

|                              |        |
|------------------------------|--------|
| Total Files Size (in bytes): | 542553 |
|------------------------------|--------|

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.

|                                                                                                                                   |                                  |                                   |
|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia                 |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

|                   |              |            |            |  |  |  |
|-------------------|--------------|------------|------------|--|--|--|
|                   | 2005/0148534 | 07/07/2005 | Castellino |  |  |  |
|                   | 2005/0164960 | 07/28/2005 | Olsen      |  |  |  |
|                   | 2005/0215513 | 09/29/2005 | Booamra    |  |  |  |
|                   | 2005/0227947 | 10/13/2005 | Chan       |  |  |  |
|                   | 2005/0261237 | 11/24/2005 | Booamra    |  |  |  |
|                   | 2006/0003951 | 01/05/2006 | Mekouar    |  |  |  |
|                   | 2006/0014943 | 01/19/2006 | Dempey     |  |  |  |
|                   | 2006/0040944 | 02/23/2006 | Gosselin   |  |  |  |
|                   | 2006/0079478 | 04/13/2006 | Booamra    |  |  |  |
|                   | 2006/0110727 | 05/25/2006 | McGall     |  |  |  |
|                   | 2006/0122146 | 06/08/2006 | Chun       |  |  |  |
| Change(s) applied | 2006/0122154 | 06/08/2006 | Olsen      |  |  |  |
| to document,      | 2007/0042939 | 02/22/2007 | LaColla    |  |  |  |
| /S.R.R./          | 60/392350    | 06/28/2002 | Storer     |  |  |  |
| 4/12/2011         | 60/392351    | 06/28/2002 | Gosselin   |  |  |  |

|                                                                                                                                                                                                                                             |                              |                 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-----------------|
| <div style="border: 1px solid black; padding: 5px; display: inline-block;"> <b>23552</b><br/> <small>PATENT TRADEMARK OFFICE</small> </div>                                                                                                 |                              |                 |
| EXAMINER                                                                                                                                                                                                                                    | /Patrick Lewis/ (12/09/2010) | 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. |                              |                 |

\*Substitute Disclosure Statement Form (PTO-1449)  
 3764190v1

|                                                                                                                                   |                                  |                                   |
|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|
| <b>FORM 1449*</b><br><b>INFORMATION DISCLOSURE STATEMENT</b><br><br><b>IN AN APPLICATION</b><br>(Use several sheets if necessary) | Docket Number:<br>60137.0034USU1 | Application Number:<br>12/053,015 |
|                                                                                                                                   | Applicant: Sofia et al.          |                                   |
|                                                                                                                                   | Filing Date: March 21, 2008      | Group Art Unit: 1623              |

| U.S. PATENT DOCUMENTS             |              |            |                                                                      |       |          |                            |
|-----------------------------------|--------------|------------|----------------------------------------------------------------------|-------|----------|----------------------------|
| EXAMINER INITIAL                  | DOCUMENT NO. | DATE       | NAME                                                                 | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                                   |              |            |                                                                      |       |          |                            |
|                                   |              |            |                                                                      |       |          |                            |
|                                   |              |            |                                                                      |       |          |                            |
|                                   |              |            |                                                                      |       |          |                            |
| U.S. PUBLISHED PATENT APPLICATION |              |            |                                                                      |       |          |                            |
| EXAMINER INITIAL                  | DOCUMENT NO. | DATE       | NAME                                                                 | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|                                   | 20010034440  | 10-25-2001 | Shepard                                                              |       |          |                            |
|                                   | 20090137521  | 05-28-2009 | Hamilton<br>(corresponds to WO2009052287)                            |       |          |                            |
|                                   | 20090233879  | 09-17-2009 | Reddy (corresponds to WO2009115893)                                  |       |          |                            |
|                                   | 20090280084  | 11-12-2009 | Schinazi<br>(corresponds to WO2009129120)                            |       |          |                            |
|                                   | 20090306007  | 12-10-2009 | Wagner                                                               |       |          |                            |
|                                   | 20100029008  | 02-04-2010 | <del>Stutz</del> Rojas Stutz et al.<br>(corresponds to WO2006063717) |       |          |                            |
|                                   | 20100035835  | 02-11-2010 | Narjes (corresponds to WO2008085508)                                 |       |          |                            |
|                                   | 20100137576  | 06-03-2010 | Stec (corresponds to WO2008048128)                                   |       |          |                            |
|                                   | 20100173863  | 07-08-2010 | Schinazi                                                             |       |          |                            |
|                                   | 20100227801  | 09-09-2010 | Hopkins<br>(corresponds to WO2010080878)                             |       |          |                            |
|                                   |              |            |                                                                      |       |          |                            |
|                                   |              |            |                                                                      |       |          |                            |
|                                   |              |            |                                                                      |       |          |                            |

Change(s) applied  
to document,  
/S.R.R./  
4/12/2011

|                                                                                                                                                                                                                                             |                 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| <b>23552</b><br>PATENT TRADEMARK OFFICE                                                                                                                                                                                                     |                 |
| EXAMINER<br>/Patrick Lewis/ (01/03/2011)                                                                                                                                                                                                    | 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. |                 |



# 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. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 12/053,015      | 03/21/2008  | MICHAEL JOSEPH SOFIA | 60137.0034USU1      | 3454             |

23552 7590 04/13/2011  
MERCHANT & GOULD PC  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-0903

|          |
|----------|
| EXAMINER |
|----------|

LEWIS, PATRICK T

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

1623

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

04/13/2011

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.

|                                           |                        |                     |
|-------------------------------------------|------------------------|---------------------|
| <b>Response to Rule 312 Communication</b> | <b>Application No.</b> | <b>Applicant(s)</b> |
|                                           | 12/053,015             | SOFIA ET AL.        |
|                                           | <b>Examiner</b>        | <b>Art Unit</b>     |
|                                           | PATRICK LEWIS          | 1623                |

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

1. ☒ The amendment filed on 01 April 2011 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

OK TO ENTER: /P.L./ (04/10/2011)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|               |                                     |                   |                   |
|---------------|-------------------------------------|-------------------|-------------------|
| Applicant:    | Michael J. Sofia et al.             | Examiner:         | LEWIS, PATRICK T. |
| Serial No.:   | 12/053,015                          | Group Art Unit:   | 1623              |
| Filed:        | March 21, 2008                      | Docket No.:       | 60137.0034USU1    |
| Customer No.: | 23552                               | Confirmation No.: | 3454              |
| Title:        | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                   |                   |

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RULE 312 AMENDMENT

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

Dear Sir:

Further to the Notice Allowability dated January 5, 2011, Applicants request that the Examiner act on the concurrently filed Rule 48(b) – Request to Correct Inventorship before the allowed application issues as a U.S. patent and enter the present amendment prior to issuance of the claims.

**Amendments to the Claims** begin on page 2 of this paper.

**Remarks** begin on page 7 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. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 12/053,015      | 03/21/2008  | MICHAEL JOSEPH SOFIA | 60137.0034USU1      | 3454             |

23552 7590 04/18/2011  
MERCHANT & GOULD PC  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-0903

|          |
|----------|
| EXAMINER |
|----------|

LEWIS, PATRICK T

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

1623

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

04/18/2011

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.



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U.S. Patent and Trademark Office  
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Alexandria, Virginia 22313-1450

| APPLICATION NO./<br>CONTROL NO. | FILING DATE | FIRST NAMED INVENTOR /<br>PATENT IN REEXAMINATION | ATTORNEY DOCKET NO. |
|---------------------------------|-------------|---------------------------------------------------|---------------------|
| 12/053,015                      | 3/21/2008   | Michael J. Sofia et al.                           | 60137.0034USU1      |

Merchant & Gould PC  
P.O. Box 2903  
Minneapolis, MN 55402-0903  
United States

EXAMINER

Patrick Lewis

| ART UNIT | PAPER     |
|----------|-----------|
| 1623     | 20110410A |

DATE MAILED:

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

Commissioner for Patents

This is in response to the petition under 37 CFR 1.48(b), filed April 1, 2011, requesting that Dhanapalan Nagarathnam be deleted as an inventor from the above-identified application.

Amendment of the inventorship requires:

- (1) A request, signed by a party set forth in § 1.33(b), to correct the inventorship that identifies the named inventor or inventors being deleted and acknowledges that the inventor's invention is no longer being claimed in the nonprovisional application; and
- (2) The processing fee set forth in § 1.17(i).

The petition and case history has been considered carefully.

The petition, signed by Daniel R. Evans, which removes Dhanapalan Nagarathnam as an inventor satisfies the requirement (1) that a request be signed by a party set forth in § 1.33(b) and the submission of the processing fee satisfies 37 CFR 1.48(b). Therefore, the requirements for a grantable petition under 37 CFR 1.48(b) have been satisfied.

The petition to delete Dhanapalan Nagarathnam as an inventor under 37 CFR 1.48(b) is GRANTED.

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



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Bib Data Sheet

CONFIRMATION NO. 3454

|                                                                                                                                                                                                                                                                                                   |                                                                                                                   |                               |                                                                                                                                                                                                                                                                                 |                                              |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| <b>SERIAL NUMBER</b><br>12/053,015                                                                                                                                                                                                                                                                | <b>FILING OR 371(c) DATE</b><br>03/21/2008<br><b>RULE</b>                                                         | <b>CLASS</b><br>514           | <b>GROUP ART UNIT</b><br>1623                                                                                                                                                                                                                                                   | <b>ATTORNEY DOCKET NO.</b><br>60137.0034USU1 |
| <b>APPLICANTS</b><br>MICHAEL JOSEPH SOFIA, Doylestown, PA;<br>JINFA DU, New Hope, PA;<br>PEIYUAN WANG, Glen Rock, NJ;                                                                                                                                                                             |                                                                                                                   |                               |                                                                                                                                                                                                                                                                                 |                                              |
| <b>** CONTINUING DATA *****</b><br>This appln claims benefit of 60/909,315 03/30/2007<br>and claims benefit of 60/982,309 10/24/2007                                                                                                                                                              |                                                                                                                   |                               |                                                                                                                                                                                                                                                                                 |                                              |
| <b>** FOREIGN APPLICATIONS *****</b>                                                                                                                                                                                                                                                              |                                                                                                                   |                               |                                                                                                                                                                                                                                                                                 |                                              |
| <b>IF REQUIRED, FOREIGN FILING LICENSE GRANTED** SMALL ENTITY **</b><br>** 05/01/2008                                                                                                                                                                                                             |                                                                                                                   |                               |                                                                                                                                                                                                                                                                                 |                                              |
| Foreign Priority claimed <input type="checkbox"/> yes <input type="checkbox"/> no<br>35 USC 119 (a-d) conditions <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> Met after<br>met Allowance<br>Verified and Acknowledged _____<br>Examiner's Signature Initials |                                                                                                                   | <b>STATE OR COUNTRY</b><br>PA | <b>SHEETS DRAWING</b><br>0                                                                                                                                                                                                                                                      | <b>TOTAL CLAIMS</b><br>12                    |
|                                                                                                                                                                                                                                                                                                   |                                                                                                                   |                               |                                                                                                                                                                                                                                                                                 | <b>INDEPENDENT CLAIMS</b><br>12              |
| <b>ADDRESS</b><br>23552                                                                                                                                                                                                                                                                           |                                                                                                                   |                               |                                                                                                                                                                                                                                                                                 |                                              |
| <b>TITLE</b><br>NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS                                                                                                                                                                                                                                               |                                                                                                                   |                               |                                                                                                                                                                                                                                                                                 |                                              |
| <b>FILING FEE RECEIVED</b><br>3071                                                                                                                                                                                                                                                                | FEES: Authority has been given in Paper<br>No. _____ to charge/credit DEPOSIT ACCOUNT<br>No. _____ for following: |                               | <input type="checkbox"/> All Fees<br><input type="checkbox"/> 1.16 Fees ( Filing )<br><input type="checkbox"/> 1.17 Fees ( Processing Ext. of time )<br><input type="checkbox"/> 1.18 Fees ( Issue )<br><input type="checkbox"/> Other _____<br><input type="checkbox"/> Credit |                                              |



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[www.uspto.gov](http://www.uspto.gov)

| APPLICATION NO. | ISSUE DATE | PATENT NO. | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|------------|------------|---------------------|------------------|
| 12/053,015      | 06/21/2011 | 7964580    | 60137,0034USU1      | 3454             |

23552 7590 06/01/2011  
MERCHANT & GOULD PC  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-0903

## 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 370 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;

03956.053800.

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.: 12/053,015 | ) |                            |
|                             | : | Confirmation No.: 3454     |
| Filed: March 21, 2008       | ) |                            |
|                             | : |                            |
| 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

FCHS\_WS 7658010v1.doc

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 12612228                            |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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:              | 60137.0034USU1                      |
| Receipt Date:                        | 24-APR-2012                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 12:15:47                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description | File Name          | File Size(Bytes)/<br>Message Digest                            | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|--------------------|----------------------------------------------------------------|------------------|------------------|
| 1               | Power of Attorney    | 03956053800poa.pdf | 112385<br><small>(2e110380c897107a0c43a70e1500cc46305)</small> | 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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Alexandria, Virginia 22313-1450  
www.uspto.gov

| APPLICATION NUMBER | FILING OR 371(C) DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO./TITLE |
|--------------------|-----------------------|-----------------------|------------------------|
| 12/053,015         | 03/21/2008            | MICHAEL JOSEPH SOFIA  | 60137.0034USU1         |

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

**CONFIRMATION NO. 3454**  
**POA ACCEPTANCE LETTER**



Date Mailed: 05/03/2012

**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



UNITED STATES PATENT AND TRADEMARK OFFICE

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www.uspto.gov

| APPLICATION NUMBER | FILING OR 371(C) DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO./TITLE |
|--------------------|-----------------------|-----------------------|------------------------|
| 12/053,015         | 03/21/2008            | MICHAEL JOSEPH SOFIA  | 60137.0034USU1         |

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

**CONFIRMATION NO. 3454**  
**POWER OF ATTORNEY NOTICE**



Date Mailed: 05/03/2012

**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

### "FEE ADDRESS" INDICATION FORM

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

Fax to:  
571-273-6500

- OR -

**INSTRUCTIONS:** The issue fee must have been paid for application(s) listed on this form. In addition, only an address represented by a Customer Number can be established as the fee address for maintenance fee purposes (hereafter, fee address). A fee address should be established when correspondence related to maintenance fees should be mailed to a different address than the correspondence address for the application. **When to check the first box below:** If you have a Customer Number to represent the fee address. **When to check the second box below:** If you have no Customer Number representing the desired fee address, in which case a completed Request for Customer Number (PTO/SB/125) must be attached to this form. For more information on Customer Numbers, see the Manual of Patent Examining Procedure (MPEP) § 403.

For the following listed application(s), please recognize as the "Fee Address" under the provisions of 37 CFR 1.363 the address associated with:

☒ Customer Number: 25000

OR

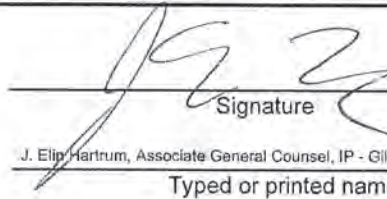
☐ The attached Request for Customer Number (PTO/SB/125) form.

| PATENT NUMBER<br>(if known) | APPLICATION NUMBER |
|-----------------------------|--------------------|
| 7,964,580                   | 12/053,015         |

Completed by (check one):

☐ Applicant/Inventor

☐ Attorney or Agent of record 43,663  
(Reg. No.)

  
Signature  
J. Elip Hartum, Associate General Counsel, IP - Gilead Pharmasset LLC  
Typed or printed name

☒ 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)

650-574-3000  
Requester's telephone number

☐ Assignee recorded at Reel \_\_\_\_\_ Frame \_\_\_\_\_

MARCH 6, 2013  
Date

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 1 forms are submitted.

This collection of information is required by 37 CFR 1.363. 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 5 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 COMPLETE D FORMS TO THIS ADDRESS.  
SEND TO: Mail Stop M Correspondence, 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.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

**STATEMENT UNDER 37 CFR 3.73(b)**

Applicant/Patent Owner: Michael Joseph Sofia et al.  
 Application No./Patent No.: 7,964,580 Filed/Issue Date: June 21, 2011  
 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. ☐ an 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 thereof 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:

- Michael Joseph Sofia, Jinfa Du,  
 Peiyuan Wang,  
 1. From: Dhanapalan Nagarathnam To: Pharmasset, Inc.  
 The document was recorded in the United States Patent and Trademark Office at  
 Reel 020739, Frame 0883, 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.

J. Elin Hartrum  
 Signature  
J. Elin Hartrum  
 Printed or Typed Name

MARCH 6, 2013  
 Date  
Associate General Counsel, IP  
 Title

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

Dated: 3/7/2013 Signature: Donna Macedo (Donna Macedo)

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 15144106                            |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| Title of Invention:                  | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |
| First Named Inventor/Applicant Name: | MICHAEL JOSEPH SOFIA                |
| Customer Number:                     | 104538                              |
| Filer:                               | Jenny Elin Hartrum/Donna Macedo     |
| Filer Authorized By:                 | Jenny Elin Hartrum                  |
| Attorney Docket Number:              | 03956.053800.                       |
| Receipt Date:                        | 07-MAR-2013                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 14:30:12                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description          | File Name                                                                 | File Size(Bytes)/<br>Message Digest           | Multi Part /.zip | Pages (if appl.) |
|-----------------|-------------------------------|---------------------------------------------------------------------------|-----------------------------------------------|------------------|------------------|
| 1               | Miscellaneous Incoming Letter | PH3080PC_2013-03-07_NtfcOf<br>LossOfEntitlemntToSmallEntity<br>Status.pdf | 52659<br>ad1885990e32a563031c29539230867d174c | no               | 1                |

### Warnings:

### Information:

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                   |                                                      |                                                                        |    |   |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|------------------------------------------------------|------------------------------------------------------------------------|----|---|
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Change of Address                                 | PH3080PC_2013-03-07_FeeAd<br>dressIndicationForm.pdf | 109642<br><small>2716246a37866a764c861d9143efc5e311c<br/>11627</small> | no | 1 |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                   |                                                      |                                                                        |    |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                   |                                                      |                                                                        |    |   |
| 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Assignee showing of ownership per 37<br>CFR 3.73. | PH3080PC_2013-03-07_Statem<br>entUnder373b.pdf       | 83045<br><small>509b769411ba9931dc97c2b5a3814ee813<br/>4460</small>    | no | 1 |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                   |                                                      |                                                                        |    |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                   |                                                      |                                                                        |    |   |
| <b>Total Files Size (in bytes):</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                   |                                                      | 245346                                                                 |    |   |
| <p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |                                                   |                                                      |                                                                        |    |   |

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

Dated: 3/7/2013 Signature: D. Macedo  
(Donna Macedo)

Docket No. PH3080.PC

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Michael Joseph Sofia et al.

Patent No.: 7,964,580  
Issued: June 21, 2011

Confirmation No.: 3454  
Art Unit: 1623

Application No. 12/053,015  
File Date: March 21, 2008

For: Nucleoside Phosphoramidate Prodrugs Examiner: Lewis, Patrick T.

**NOTIFICATION OF LOSS OF ENTITLEMENT TO SMALL ENTITY STATUS**

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

Dear Madam:

Assignee, Gilead Pharmasset LLC, hereby notifies the Patent and Trademark Office that it is not entitled to status as a small entity, and that the claim for small entity status filed by the Applicant is hereby withdrawn.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 07-1250, under Order No. PH3080.PC from which the undersigned is authorized to draw.

Dated: MARCH 6, 2013

Respectfully submitted,

By J. Elin Hartrum  
J. Elin Hartrum  
Registration No.: 43,663  
GILEAD PHARMASSET LLC  
Correspondence Customer Number: 25000  
Attorney For Applicant

## 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

|                                                  |       |     |       |
|--------------------------------------------------|-------|-----|-------|
| <input type="checkbox"/> Firm or Individual Name |       |     |       |
| Address                                          |       |     |       |
| City                                             | State | Zip |       |
| Country                                          |       |     |       |
| Telephone                                        |       |     | Email |

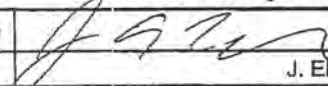
Assignee Name and Address:

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.: 7,964,580

Filed/Issue Date: 06/21/2011

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 020739, Frame 0883, 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

NThakur

Date

6/20/2014

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

Agent for Applicant

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.

| Electronic Acknowledgement Receipt   |                                      |
|--------------------------------------|--------------------------------------|
| EFS ID:                              | 19485150                             |
| Application Number:                  | 12053015                             |
| International Application Number:    |                                      |
| Confirmation Number:                 | 3454                                 |
| 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.                        |
| Receipt Date:                        | 02-JUL-2014                          |
| Filing Date:                         | 21-MAR-2008                          |
| Time Stamp:                          | 19:58:38                             |
| Application Type:                    | Utility under 35 USC 111(a)          |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description | File Name              | File Size(Bytes)/<br>Message Digest                | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|------------------------|----------------------------------------------------|------------------|------------------|
| 1               |                      | POA-STMT-199059-US.pdf | 299464<br>2840828b351ec06c79a191b3046ac62729c99-29 | 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:**

|                                     |        |
|-------------------------------------|--------|
| <b>Total Files Size (in bytes):</b> | 299464 |
|-------------------------------------|--------|

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 |
|--------------------|-----------------------|-----------------------|------------------------|
| 12/053,015         | 03/21/2008            | MICHAEL JOSEPH SOFIA  | 03956.053800.          |

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

**CONFIRMATION NO. 3454**  
**POWER OF ATTORNEY NOTICE**



Date Mailed: 07/10/2014

**NOTICE REGARDING CHANGE OF POWER OF ATTORNEY**

This is in response to the Power of Attorney filed 07/02/2014.

- 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).

/ltaba/

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 |
|--------------------|-----------------------|-----------------------|------------------------|
| 12/053,015         | 03/21/2008            | MICHAEL JOSEPH SOFIA  | 03956.053800.          |

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

**CONFIRMATION NO. 3454**  
**POA ACCEPTANCE LETTER**



Date Mailed: 07/10/2014

## NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 07/02/2014.

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.

/Itaba/

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

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.

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

|                        |                      |
|------------------------|----------------------|
| Patent Number          | 7,964,580            |
| Issue Date             | 06-21-2011           |
| Application Number     | 12/053,015           |
| Filing Date            | 03-21-2008           |
| First Named Inventor   | Michael Joseph SOFIA |
| Attorney Docket Number | 37JD-199059-US       |

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. TannerDate 03-31-2015Telephone 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:                              | 21934090                            |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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-US                      |
| Receipt Date:                        | 31-MAR-2015                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 18:06:18                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description | File Name                                          | File Size(Bytes)/<br>Message Digest              | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|----------------------------------------------------|--------------------------------------------------|------------------|------------------|
| 1               | Change of Address    | PH3080PC_ChangeOfCorrespondence_37JD-199059-US.pdf | 157125<br>7b2063f6e01350a0c27e410d3752ba0b410345 | 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.

|                                                                                                                                                            |                        |                                        |
|------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|----------------------------------------|
| <b>PATENT - POWER OF ATTORNEY<br/>OR<br/>REVOCATION OF POWER OF ATTORNEY<br/>WITH A NEW POWER OF ATTORNEY<br/>AND<br/>CHANGE OF CORRESPONDENCE ADDRESS</b> | Patent Number          | 7,984,580                              |
|                                                                                                                                                            | Issue Date             | 06/21/2011                             |
|                                                                                                                                                            | First Named Inventor   | Michael Joseph SOPA                    |
|                                                                                                                                                            | Title                  | NUCLEOSIDE PHOSPHORAMIDATE<br>PRODRUGS |
|                                                                                                                                                            | Attorney Docket Number | PH3080.PC                              |

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: 124953

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:

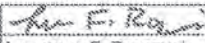
I am the:

☐ Inventor, having ownership of the patent.

OR

☒ Patent owner.  
Statement under 37 CFR 3.73(b) (Form PTO/SB/96) submitted herewith or filed on \_\_\_\_\_

SIGNATURE of Inventor or Patent Owner

|                   |                                                                                     |           |                |
|-------------------|-------------------------------------------------------------------------------------|-----------|----------------|
| Signature         |  | Date      | April 03, 2015 |
| Name              | Lawrence F. Rozsnyai                                                                | Telephone | 415-205-9836   |
| Title and Company | Patent Counsel, Gilead Pharmasset LLC                                               |           |                |

NOTE: Signatures of all the inventors or patent owners of the entire interest or their representatives 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.

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

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 21963938                            |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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-US                      |
| Receipt Date:                        | 03-APR-2015                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 11:57:29                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description | File Name                                         | File Size(Bytes)/<br>Message Digest                   | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|---------------------------------------------------|-------------------------------------------------------|------------------|------------------|
| 1               |                      | PH3080PC_2015_04_02_State<br>ment373_as_Filed.PDF | 218684<br>917091172d180326757113552d988894b-<br>b3250 | 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:**

|                                     |        |
|-------------------------------------|--------|
| <b>Total Files Size (in bytes):</b> | 218684 |
|-------------------------------------|--------|

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.: 7,964,580

Filed/Issue Date: 06-21-2011

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 020739, Frame 0883, 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 0886, 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, 2015

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 this form, call 1-800-PTO-9198 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 |
|--------------------|-----------------------|-----------------------|------------------------|
| 12/053,015         | 03/21/2008            | MICHAEL JOSEPH SOFIA  | 371D-199059-US         |

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

**CONFIRMATION NO. 3454**  
**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).

/s/dinh/

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 |
|--------------------|-----------------------|-----------------------|------------------------|
| 12/053,015         | 03/21/2008            | MICHAEL JOSEPH SOFIA  | PH3080.PC              |

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

**CONFIRMATION NO. 3454**  
**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.

/dtdinh/

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

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Inventor(s): Michael Joseph Sofia et al.

Patent No.: 7,964,580

Issued: June 21, 2011

For: NUCLEOSIDE PHOSPHORAMIDATE  
PRODRUGS

---

**REQUEST FOR CERTIFICATE OF CORRECTION  
PURSUANT TO 37 C.F.R. § 1.322**

Office of Data Management Attention: Certificates of Correction Branch  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Commissioner:

Upon reviewing the above-identified U.S. patent, Patentee noted a printing error by the U.S. Patent and Trademark Office which should be corrected. Pursuant to the provisions of 37 C.F.R. §1.322, Applicant respectfully requests correction by the Patent Office of the captioned patent and submits the attached form PTO/SB/44.

On the Front Page:

Before the heading "Int. Cl.," column 1, item 51 of the patent, please insert:

**--Related U.S. Application Data**

Provisional Application No. 60/909,315, filed March 30, 2007 and Provisional  
Application No. 60/982,309, filed October 24, 2007.--

Applicant respectfully submits that the correct priority claim is reflected in the Official Filing Receipt mailed on August 19, 2008, and Application Data Sheet submitted on March 21, 2008.

Patent No.: 7,964,580

Docket No.: 37JD-199059-US

It is respectfully requested that the attached Form PTO/SB/44 be certified and returned to the undersigned attorney at the earliest convenience of the Office.

As the error was on the part of the Patent Office, it is believed that no fees are due in connection with the submission of these papers. However, if a fee is required, the Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 50-6219.

Respectfully submitted,

Dated: March 17, 2017

By /Neeta C. Thakur/  
Neeta C. Thakur, Ph.D.  
Registration No.: 59,123  
Attorney for Applicant  
SHEPPARD MULLIN RICHTER & HAMPTON LLP  
379 Lytton Avenue  
Palo Alto, California 94301  
(650) 815-2631  
Customer Number: 117796

**UNITED STATES PATENT AND TRADEMARK OFFICE  
CERTIFICATE OF CORRECTION**

Page 1 of 1

PATENT NO. : 7,964,580  
APPLICATION NO. : 12/053,015  
ISSUE DATE : June 21, 2011  
INVENTOR(S) : Michael Joseph Sofia et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the Front Page:

Before the heading "Int. Cl.," column 1, item 51 of the patent, please insert:

**--Related U.S. Application Data**

Provisional Application No. 60/909,315, filed March 30, 2007 and Provisional  
Application No. 60/982,309, filed October 24, 2007.--

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Neeta C. Thakur  
SHEPPARD MULLIN RICHTER & HAMPTON LLP  
379 Lytton Avenue  
Palo Alto, California 94301

481828630v.1 37JD-199059-US

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 28661308                            |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| Title of Invention:                  | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |
| First Named Inventor/Applicant Name: | MICHAEL JOSEPH SOFIA                |
| Customer Number:                     | 124963                              |
| Filer:                               | Neeta C. Thakur/Joannah Laluces     |
| Filer Authorized By:                 | Neeta C. Thakur                     |
| Attorney Docket Number:              | PH3080.PC                           |
| Receipt Date:                        | 17-MAR-2017                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 18:02:10                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description                  | File Name                                                | File Size(Bytes)/ Message Digest                 | Multi Part /.zip | Pages (if appl.) |
|-----------------|---------------------------------------|----------------------------------------------------------|--------------------------------------------------|------------------|------------------|
| 1               | Request for Certificate of Correction | 37JD-199059-US_Request_for_Certificate_of_Correction.pdf | 92231<br>e80585b9a1d355513408f626d2f0326cc0a5176 | no               | 2                |

### Warnings:

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                               |                                                      |                                        |        |   |
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| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                               |                                                      |                                        |        |   |
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Miscellaneous Incoming Letter | 37JD-199059-<br>US_Certificate_of_Correction.<br>pdf | 119488                                 | no     | 1 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                               |                                                      | 5f1cc55f058216c571ee2a6102cd1122170355 |        |   |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                               |                                                      |                                        |        |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                               |                                                      |                                        |        |   |
| Total Files Size (in bytes):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                               |                                                      |                                        | 211719 |   |
| <p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/>         If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/>         If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/>         If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |                               |                                                      |                                        |        |   |

## 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

|                                                  |       |     |  |
|--------------------------------------------------|-------|-----|--|
| <input type="checkbox"/> Firm or Individual Name |       |     |  |
| Address                                          |       |     |  |
| City                                             | State | Zip |  |
| Country                                          |       |     |  |
| Telephone                                        | Email |     |  |

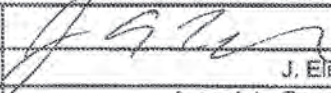
Assignee Name and Address:

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.

## Privacy Act Statement

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

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

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

**STATEMENT UNDER 37 CFR 3.73(b)**Applicant/Patent Owner: Gilead Pharmasset LLCApplication No./Patent No.: 7,964,580 Filed/Issue Date: June 21, 2011Titled: 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 020739, Frame 0883, 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  
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3. From: \_\_\_\_\_ To: \_\_\_\_\_  
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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

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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                     |                        |                                                  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|------------------------|--------------------------------------------------|
| <b>Application Data Sheet 37 CFR 1.76</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                     | Attorney Docket Number | <del>60437-0034-USU4</del> <b>37JD-199059-US</b> |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                     | Application Number     | <b>12/053,015</b>                                |
| Title of Invention                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                        |                                                  |
| <p>The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.</p> <p>This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.</p> |                                     |                        |                                                  |

**Secrecy Order 37 CFR 5.2**

- ☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

**Applicant Information:**

|                                                                                                                                                                                 |                   |                                           |                    |                                                                |                                                             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-------------------------------------------|--------------------|----------------------------------------------------------------|-------------------------------------------------------------|
| <b>Applicant 1</b>                                                                                                                                                              |                   |                                           |                    |                                                                | <a href="#">Remove</a>                                      |
| <b>Applicant Authority</b>                                                                                                                                                      |                   | <input checked="" type="radio"/> Inventor |                    | <input type="radio"/> Legal Representative under 35 U.S.C. 117 | <input type="radio"/> Party of Interest under 35 U.S.C. 118 |
| <b>Prefix</b>                                                                                                                                                                   | <b>Given Name</b> | <b>Middle Name</b>                        | <b>Family Name</b> | <b>Suffix</b>                                                  |                                                             |
|                                                                                                                                                                                 | MICHAEL           | JOSEPH                                    | SOFIA              |                                                                |                                                             |
| <b>Residence Information (Select One)</b> <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service |                   |                                           |                    |                                                                |                                                             |
| <b>City</b>                                                                                                                                                                     | DOYLESTOWN        | <b>State/Province</b>                     | PA                 | <b>Country of Residence i</b>                                  | US                                                          |
| <b>Citizenship under 37 CFR 1.41(b) i</b>                                                                                                                                       |                   | US                                        |                    |                                                                |                                                             |
| <b>Mailing Address of Applicant:</b>                                                                                                                                            |                   |                                           |                    |                                                                |                                                             |
| <b>Address 1</b>                                                                                                                                                                |                   | 3066 ANTLER DRIVE                         |                    |                                                                |                                                             |
| <b>Address 2</b>                                                                                                                                                                |                   |                                           |                    |                                                                |                                                             |
| <b>City</b>                                                                                                                                                                     | DOYLESTOWN        | <b>State/Province</b>                     | PA                 |                                                                |                                                             |
| <b>Postal Code</b>                                                                                                                                                              | 18902             | <b>Country i</b>                          | US                 |                                                                |                                                             |
| <b>Applicant 2</b>                                                                                                                                                              |                   |                                           |                    |                                                                | <a href="#">Remove</a>                                      |
| <b>Applicant Authority</b>                                                                                                                                                      |                   | <input checked="" type="radio"/> Inventor |                    | <input type="radio"/> Legal Representative under 35 U.S.C. 117 | <input type="radio"/> Party of Interest under 35 U.S.C. 118 |
| <b>Prefix</b>                                                                                                                                                                   | <b>Given Name</b> | <b>Middle Name</b>                        | <b>Family Name</b> | <b>Suffix</b>                                                  |                                                             |
|                                                                                                                                                                                 | JINFA             |                                           | DU                 |                                                                |                                                             |
| <b>Residence Information (Select One)</b> <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service |                   |                                           |                    |                                                                |                                                             |
| <b>City</b>                                                                                                                                                                     | NEW HOPE          | <b>State/Province</b>                     | PA                 | <b>Country of Residence i</b>                                  | US                                                          |
| <b>Citizenship under 37 CFR 1.41(b) i</b>                                                                                                                                       |                   | US                                        |                    |                                                                |                                                             |
| <b>Mailing Address of Applicant:</b>                                                                                                                                            |                   |                                           |                    |                                                                |                                                             |
| <b>Address 1</b>                                                                                                                                                                |                   | 1206 REINS CIRCLE                         |                    |                                                                |                                                             |
| <b>Address 2</b>                                                                                                                                                                |                   |                                           |                    |                                                                |                                                             |
| <b>City</b>                                                                                                                                                                     | NEW HOPE          | <b>State/Province</b>                     | PA                 |                                                                |                                                             |
| <b>Postal Code</b>                                                                                                                                                              | 18938             | <b>Country i</b>                          | US                 |                                                                |                                                             |
| <b>Applicant 3</b>                                                                                                                                                              |                   |                                           |                    |                                                                | <a href="#">Remove</a>                                      |
| <b>Applicant Authority</b>                                                                                                                                                      |                   | <input checked="" type="radio"/> Inventor |                    | <input type="radio"/> Legal Representative under 35 U.S.C. 117 | <input type="radio"/> Party of Interest under 35 U.S.C. 118 |
| <b>Prefix</b>                                                                                                                                                                   | <b>Given Name</b> | <b>Middle Name</b>                        | <b>Family Name</b> | <b>Suffix</b>                                                  |                                                             |
|                                                                                                                                                                                 | PEIYUAN           |                                           | WANG               |                                                                |                                                             |
| <b>Residence Information (Select One)</b> <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service |                   |                                           |                    |                                                                |                                                             |
| <b>City</b>                                                                                                                                                                     | GLEN ROCK         | <b>State/Province</b>                     | NJ                 | <b>Country of Residence i</b>                                  | US                                                          |

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|                                           |                                     |                        |                                                 |
|-------------------------------------------|-------------------------------------|------------------------|-------------------------------------------------|
| <b>Application Data Sheet 37 CFR 1.76</b> |                                     | Attorney Docket Number | <del>00137-003-1000</del> <b>37JD-199059-US</b> |
|                                           |                                     | Application Number     | <b>12/053,015</b>                               |
| Title of Invention                        | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                        |                                                 |

|                                                                                                                                                                          |                       |                                                                |                                       |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------------------------------------------------------------|---------------------------------------|
| Citizenship under 37 CFR 1.41(b) i                                                                                                                                       |                       | CN                                                             |                                       |
| Mailing Address of Applicant:                                                                                                                                            |                       |                                                                |                                       |
| Address 1                                                                                                                                                                |                       | 20 RADBURN ROAD                                                |                                       |
| Address 2                                                                                                                                                                |                       |                                                                |                                       |
| City                                                                                                                                                                     | GLEN ROCK             | State/Province                                                 | NJ                                    |
| Postal Code                                                                                                                                                              | 07452                 | Country i                                                      | US                                    |
| Applicant 4                                                                                                                                                              |                       |                                                                | <input type="button" value="Remove"/> |
| Applicant Authority <input checked="" type="radio"/> Inventor                                                                                                            |                       | <input type="radio"/> Legal Representative under 35 U.S.C. 117 |                                       |
|                                                                                                                                                                          |                       | <input type="radio"/> Party of Interest under 35 U.S.C. 118    |                                       |
| Prefix                                                                                                                                                                   | Given Name            | Middle Name                                                    | Family Name                           |
|                                                                                                                                                                          | <del>DHANAPALAN</del> |                                                                | <del>NAGARATHNAM</del>                |
| Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service |                       |                                                                |                                       |
| City                                                                                                                                                                     | <del>BETHANY</del>    | State/Province                                                 | <del>CT</del>                         |
| Country of Residence i                                                                                                                                                   |                       | <del>US</del>                                                  |                                       |
| Citizenship under 37 CFR 1.41(b) i                                                                                                                                       |                       | <del>US</del>                                                  |                                       |
| Mailing Address of Applicant:                                                                                                                                            |                       |                                                                |                                       |
| Address 1                                                                                                                                                                |                       | <del>52 VIRGINIA RAIL DRIVE</del>                              |                                       |
| Address 2                                                                                                                                                                |                       |                                                                |                                       |
| City                                                                                                                                                                     | <del>BETHANY</del>    | State/Province                                                 | <del>CT</del>                         |
| Postal Code                                                                                                                                                              | <del>06524</del>      | Country i                                                      | <del>US</del>                         |
| All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button.                                     |                       |                                                                | <input type="button" value="Add"/>    |

**Correspondence Information:**

|                                                                                                                                       |                                                                                                                                                                 |
|---------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Enter either Customer Number or complete the Correspondence Information section below.<br>For further information see 37 CFR 1.33(a). |                                                                                                                                                                 |
| <input type="checkbox"/> An Address is being provided for the correspondence Information of this application.                         |                                                                                                                                                                 |
| Customer Number                                                                                                                       | <del>23552</del> <b>117796</b>                                                                                                                                  |
| Email Address                                                                                                                         | <del>devano@merckantigold.com</del> <b>svipdocketing@sheppardmulin.com</b> <input type="button" value="Add Email"/> <input type="button" value="Remove Email"/> |

**Application Information:**

|                                         |                                                 |                                           |                                     |
|-----------------------------------------|-------------------------------------------------|-------------------------------------------|-------------------------------------|
| Title of the Invention                  | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS             |                                           |                                     |
| Attorney Docket Number                  | <del>00137-003-1000</del> <b>37JD-199059-US</b> | Small Entity Status Claimed               | <input checked="" type="checkbox"/> |
| Application Type                        | Nonprovisional                                  |                                           |                                     |
| Subject Matter                          | Utility                                         |                                           |                                     |
| Suggested Class (if any)                |                                                 | Sub Class (if any)                        |                                     |
| Suggested Technology Center (if any)    |                                                 |                                           |                                     |
| Total Number of Drawing Sheets (if any) |                                                 | Suggested Figure for Publication (if any) |                                     |

|                                                            |                        |                                                 |
|------------------------------------------------------------|------------------------|-------------------------------------------------|
| <b>Application Data Sheet 37 CFR 1.76</b>                  | Attorney Docket Number | <del>60137-003-1000</del> <b>37JD-199059-US</b> |
|                                                            | Application Number     | <b>12/053.015</b>                               |
| Title of Invention     NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                        |                                                 |

### Publication Information:

|                                                                                                                                                                                                                                                                                                                                                                                                                        |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input type="checkbox"/> Request Early Publication (Fee required at time of Request 37 CFR 1.219)                                                                                                                                                                                                                                                                                                                      |
| <input type="checkbox"/> <b>Request Not to Publish.</b> I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application <b>has not and will not</b> be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing. |

### Representative Information:

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                  |                                              |                                                         |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|----------------------------------------------|---------------------------------------------------------|
| Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Enter either Customer Number or complete the Representative Name section below. If both sections are completed the Customer Number will be used for the Representative Information during processing. |                                                  |                                              |                                                         |
| Please Select One:                                                                                                                                                                                                                                                                                                                                                                                                                                              | <input checked="" type="radio"/> Customer Number | <input type="radio"/> US Patent Practitioner | <input type="radio"/> Limited Recognition (37 CFR 11.9) |
| Customer Number                                                                                                                                                                                                                                                                                                                                                                                                                                                 | <del>29552</del> <b>117796</b>                   |                                              |                                                         |

### Domestic Benefit/National Stage Information:

|                                                                                                                                                                                                                                                                                                                                                                                                        |                    |                          |                          |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|--------------------------|--------------------------|
| This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78(a)(2) or CFR 1.78(a)(4), and need not otherwise be made part of the specification. |                    |                          |                          |
| Prior Application Status                                                                                                                                                                                                                                                                                                                                                                               | Pending            | <a href="#">Remove</a>   |                          |
| Application Number                                                                                                                                                                                                                                                                                                                                                                                     | Continuity Type    | Prior Application Number | Filing Date (YYYY-MM-DD) |
| <b>12/053.015</b>                                                                                                                                                                                                                                                                                                                                                                                      | non provisional of | 60909315                 | 2007-03-30               |
| Prior Application Status                                                                                                                                                                                                                                                                                                                                                                               | Pending            | <a href="#">Remove</a>   |                          |
| Application Number                                                                                                                                                                                                                                                                                                                                                                                     | Continuity Type    | Prior Application Number | Filing Date (YYYY-MM-DD) |
| <b>12/053.015</b>                                                                                                                                                                                                                                                                                                                                                                                      | non provisional of | 60982309                 | 2007-10-24               |
| Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the <b>Add</b> button.                                                                                                                                                                                                                                                                                  |                    |                          | <a href="#">Add</a>      |

### Foreign Priority Information:

|                                                                                                                                                                                                                                                                                                             |                      |                                 |                                                               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|---------------------------------|---------------------------------------------------------------|
| This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(a). |                      |                                 |                                                               |
| <a href="#">Remove</a>                                                                                                                                                                                                                                                                                      |                      |                                 |                                                               |
| Application Number                                                                                                                                                                                                                                                                                          | Country <sup>1</sup> | Parent Filing Date (YYYY-MM-DD) | Priority Claimed                                              |
|                                                                                                                                                                                                                                                                                                             |                      |                                 | <input type="radio"/> Yes <input checked="" type="radio"/> No |
| Additional Foreign Priority Data may be generated within this form by selecting the <b>Add</b> button.                                                                                                                                                                                                      |                      |                                 | <a href="#">Add</a>                                           |

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|-------------------------------------------|-------------------------------------|------------------------|--------------------------------------------------|
| <b>Application Data Sheet 37 CFR 1.76</b> |                                     | Attorney Docket Number | <del>60137-0034/US14</del> <b>37JD-199059-US</b> |
|                                           |                                     | Application Number     | <b>12/053,015</b>                                |
| Title of Invention                        | NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS |                        |                                                  |

**Assignee Information:**

Providing this information in the application data sheet does not substitute for compliance with any requirement of part 3 of Title 37 of the CFR to have an assignment recorded in the Office.

**Assignee 1**

Remove

If the Assignee is an Organization check here. ☒

Organization Name ~~PHARMASSET, INC.~~ **Gilead Pharmasset LLC**

**Mailing Address Information:**

Address 1 ~~303 A COLLEGE ROAD EAST~~ **c/o Gilead Sciences, Inc.**

Address 2 **333 Lakeside Drive**

City ~~PRINCETON~~ **Foster City** State/Province ~~HI~~ **CA**

Country US Postal Code ~~08540~~ **94404**

Phone Number Fax Number

Email Address

Additional Assignee Data may be generated within this form by selecting the Add button.

Add

**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 (YYYY-MM-DD) | 2017-04-17                 |
| First Name | Lorna L.          | Last Name | Tanner            | Registration Number 50,782 |

This collection of information is required by 37 CFR 1.76. 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 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet 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.**

| Electronic Acknowledgement Receipt   |                                     |
|--------------------------------------|-------------------------------------|
| EFS ID:                              | 28945518                            |
| Application Number:                  | 12053015                            |
| International Application Number:    |                                     |
| Confirmation Number:                 | 3454                                |
| 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.PC                           |
| Receipt Date:                        | 17-APR-2017                         |
| Filing Date:                         | 21-MAR-2008                         |
| Time Stamp:                          | 16:17:28                            |
| Application Type:                    | Utility under 35 USC 111(a)         |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description | File Name        | File Size(Bytes)/<br>Message Digest                     | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|------------------|---------------------------------------------------------|------------------|------------------|
| 1               | Power of Attorney    | 199059US_POA.pdf | 907228<br><br>1/3807a720f6694c870621f93d610618<br>da223 | no               | 7                |

### Warnings:

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

**Information:**

**Total Files Size (in bytes):**

907228

**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 |
|--------------------|-----------------------|-----------------------|------------------------|
| 12/053,015         | 03/21/2008            | MICHAEL JOSEPH SOFIA  | PH3080.PC              |

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

**CONFIRMATION NO. 3454**  
**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.

/kxaysana/



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 |
|--------------------|-----------------------|-----------------------|------------------------|
| 12/053,015         | 03/21/2008            | MICHAEL JOSEPH SOFIA  | 371D-199059-US         |

**CONFIRMATION NO. 3454**  
**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.

/kxaysana/

UNITED STATES PATENT AND TRADEMARK OFFICE  
**CERTIFICATE OF CORRECTION**

PATENT NO. : 7,964,580 B2  
APPLICATION NO. : 12/053015  
DATED : June 21, 2011  
INVENTOR(S) : Michael Joseph Sofia et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

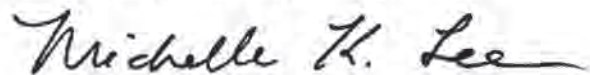
On the Title Page

Before the heading "Int. Cl.," Column I, item (51) of the patent, please insert:

**--Related U.S. Application Data**

Provisional Application No. 60/909,315, filed March 30, 2007 and Provisional Application  
No. 60/982,309, filed October 24, 2007.--

Signed and Sealed this  
Twenty-fifth Day of April, 2017



Michelle K. Lee  
*Director of the United States Patent and Trademark Office*

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.

---

IPR2018-00119  
Patent 7,964,580 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 1–14 of U.S. Patent 7,964,580 B2 (Ex. 1001, “the ’580 patent”). Paper 2 (“Pet.”). Gilead Pharmasset LLC (“Patent Owner”) filed a Preliminary Response. Paper 6 (“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 ’580 patent, IPR2018-00120. Pet., 2; Paper 4, 3. Patent Owner also identifies additional petitions filed by Petitioner for *inter partes* review of other patents owned by Patent Owner: IPR2018-00121 and IPR2018-00122 for U.S. Patent No. 8,334,270 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 '580 Patent (Ex. 1001)*

The '580 patent is directed to, *inter alia*, a phosphoramidate prodrug of a nucleoside derivative for treatment of viral infections in mammals, its ester, or a stereoisomer thereof. Ex. 1001, Abstract, 493:42–45. The '580 patent also addresses methods of treatment, uses, and processes for preparing such compounds. *Id.*, Abstract.

By way of a certificate of correction (Ex. 3001), the '580 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 provisional” and “the '309 provisional”).<sup>1</sup>

*C. Illustrative Claims*

Independent claims 1 and 8—reproduced below—are illustrative of the claimed subject matter.

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.

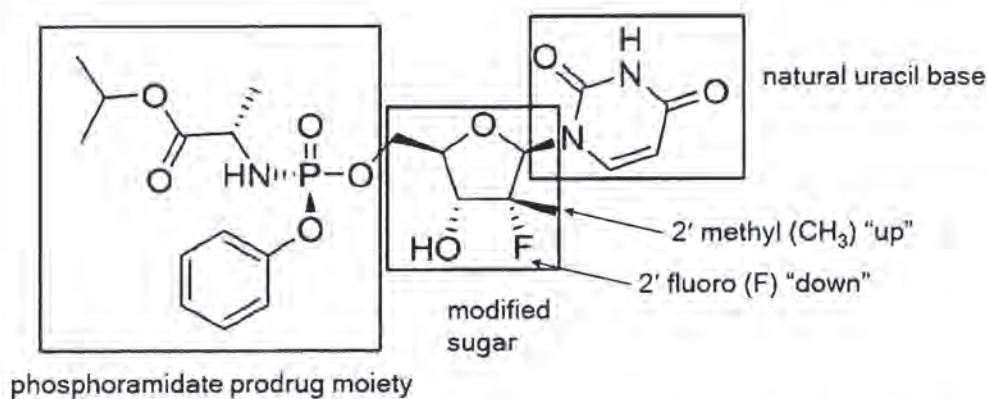
Ex. 1001, 493:42–45, 495:27–30.

Claim 8 is directed to the Sp stereoisomer (i.e., sofosbuvir), whereas claim 1 covers the Sp stereoisomer, the Rp stereoisomer, and

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<sup>1</sup> Petitioner does not contest that the '580 patent claims the benefit of priority to both the '315 provisional and the '309 provisional (Pet. 5), but rather, as discussed below, contests that the '580 patent is entitled to the claimed benefit of priority to the '315 provisional (*id.* at 23, 25).

mixtures of the two. Prelim. Resp. 3–4, 12; *see also* Pet. 28–29. The structure of sofosbuvir, as annotated by Patent Owner, is depicted below:



Prelim. Resp. 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.*

#### *D. The Asserted Grounds of Unpatentability*

Petitioner asserts that claims 1–14 of the '580 patent are unpatentable based on the following grounds. Pet. 3.

| References                     | Statutory Basis |
|--------------------------------|-----------------|
| Sofia <sup>2</sup>             | § 102           |
| Sofia and Perrone <sup>3</sup> | § 103           |
| Ma <sup>4</sup> and Perrone    | § 103           |

<sup>2</sup> 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).

<sup>3</sup> Perrone et al., 50 J. MED. CHEM. 1840–1849 (2007) (Ex. 1008).

<sup>4</sup> Ma et al., 282 J. BIOL. CHEM. 29812–29820 (2007) (Ex. 1005).

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 appear. 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 ‘580 [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 Oil 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 provisional does not describe the specific compounds claimed by the ‘580 patent in that “it does not discuss the specific compounds and stereochemistry around the phosphorous atom claimed.” Pet. 23, 25; Ex. 1002 ¶ 73. The relied on declaration testimony, reproduced below in full, states:

The ‘315 provisional application does not include a description of the specific compounds claimed by the ‘580 patent. While the ‘315 provisional discusses broad genera of compounds, it

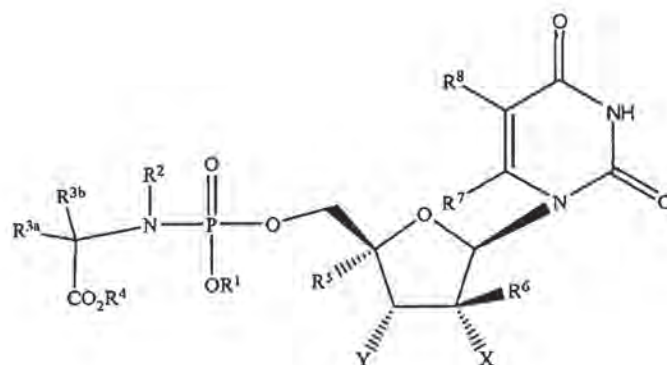
does not discuss the specific compounds and stereochemistry around the phosphorous atom claimed in the '580 patent.

Ex. 1002 ¶ 73.

Patent Owner contends the '580 patent is entitled to the benefit of priority of the '315 provisional, and that Petitioner fails to meet its burden of producing evidence that the '580 patent is not entitled to its earliest priority date. Prelim. Resp. 15. Patent Owner contends that "neither [Petitioner] nor its expert has presented a legitimate priority analysis." *Id.*

Citing specific disclosure from the '315 provisional, Patent Owner offers a detailed explanation how the '315 provisional supports Patent Owner's contention that the claims of the '580 patent are entitled to the priority benefit of the '315 provisional. *Id.* at 16–20. Patent Owner addresses chemical structure, stereochemistry, and synthesis. *Id.*

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., R<sup>1</sup>, R<sup>2</sup>, R<sup>3a</sup>, R<sup>3b</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, X, Y, R<sup>7</sup>, and R<sup>8</sup>, 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 <sup>1</sup> | R <sup>2</sup> | R <sup>3a</sup> | R <sup>3b</sup>                                   | R <sup>4</sup>  | R <sup>5</sup> | R <sup>6</sup>  | X | Y  | R <sup>7</sup> | R <sup>8</sup> |
|---------|----------------|----------------|-----------------|---------------------------------------------------|-----------------|----------------|-----------------|---|----|----------------|----------------|
| IX-25-1 | Ph             | H              | H               | H                                                 | <sup>i</sup> Pr | H              | CH <sub>3</sub> | F | OH | H              | H              |
| IX-25-2 | Ph             | H              | H               | CH <sub>3</sub>                                   | <sup>i</sup> Pr | H              | CH <sub>3</sub> | F | OH | H              | H              |
| IX-25-3 | Ph             | H              | H               | CH(CH <sub>3</sub> ) <sub>2</sub>                 | <sup>i</sup> Pr | H              | CH <sub>3</sub> | F | OH | H              | H              |
| IX-25-4 | Ph             | H              | H               | CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub> | <sup>i</sup> Pr | H              | CH <sub>3</sub> | F | OH | H              | H              |
| IX-25-5 | Ph             | H              | H               | CH <sub>2</sub> Ph                                | <sup>i</sup> Pr | H              | CH <sub>3</sub> | F | OH | H              | H              |
| IX-25-6 | Ph             | H              | H               | CH <sub>2</sub> -indol-3-yl                       | <sup>i</sup> Pr | H              | CH <sub>3</sub> | F | OH | H              | H              |
| IX-25-7 | Ph             | H              | H               | CH <sub>2</sub> CH <sub>2</sub> SCH <sub>3</sub>  | <sup>i</sup> Pr | H              | CH <sub>3</sub> | F | OH | H              | H              |
| IX-25-8 | Ph             | *              | H               | *                                                 | <sup>i</sup> Pr | H              | CH <sub>3</sub> | F | OH | H              | H              |

\*R<sup>2</sup> and R<sup>3b</sup> joined together by (CH<sub>2</sub>)<sub>3</sub> to form five-membered ring.

Prelim. Resp. 17–18; *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 at the carbon substituted with R<sup>3a</sup> and R<sup>3b</sup> 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<sup>3a</sup> and R<sup>3b</sup> and at the phosphorus (P) for each compound, including IX-25-2. Prelim Resp. 18–20 (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<sup>3a</sup> projects towards the viewer while R<sup>3b</sup> projects away from the viewer” and those in which “R<sup>3a</sup> projects away from the viewer while R<sup>3b</sup> projects towards the viewer.” *Id.* at 18–19 (emphasis omitted) (citing Ex. 2013, 63). And, as to the phosphorus (P), the compounds disclosed include those in which “the oxo-substituent projects towards the viewer while the OR<sup>1</sup> substituent projects away from the viewer, and vice versa.” *Id.* at 19–20 (citing Ex. 2013, 63–64).

In sum, the cited disclosure identifies compounds according to IX-25-2 that include both stereochemical orientations at the carbon bearing the specified R<sup>3a</sup> and R<sup>3b</sup> constituents, both stereochemical orientations at the phosphorous, and stereochemical orientations elsewhere that are identical to those of sofosbuvir. Thus, 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<sup>3a</sup> and R<sup>3b</sup> 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 of particular compounds according to the claims, we agree with Patent Owner that Petitioner fails to sufficiently demonstrate that the ’580 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 sound basis for Petitioner’s contentions that Sofia is prior art “because it was published by September 13, 2007” (Pet. 23), and that Ma is prior art “because it was published on October 12, 2007 (*id.* at 25).

*D. Alleged Unpatentability of the Challenged Claims*

*1. Anticipation by Sofia*

Petitioner asserts that claims 1–14 are anticipated by Sofia. Pet. 28–34. The unavailability of Sofia as prior art undermines Petitioner’s anticipation ground. Accordingly, we are not persuaded that Petitioner establishes a reasonable likelihood of prevailing in showing that the subject matter of claims 1–14 is unpatentable over Sofia.

*2. Obviousness over Sofia and Perrone*

Petitioner contends that claims 1–14 are unpatentable as obvious over the combination of Sofia and Perrone. *Id.* at 34–47. The unavailability of Sofia undermines Petitioner’s obviousness ground, which relies on Sofia as to the nucleoside portion of the claimed prodrug, that is, “the uridine analog ‘(2’R)-2’-deoxy-2’-fluoro-2’-C-methyluridine.’” *Id.* at 35. Perrone, relied on as to the phosphoramidate portion of the prodrug (*id.* at 39–43), uses a different uridine analog, 4'-azidouridine (Ex. 1008). Accordingly, we are not persuaded that Petitioner establishes a reasonable likelihood of prevailing in showing that the subject matter of claims 1–14 is unpatentable over Sofia and Perrone.

3. *Obviousness over Ma and Perrone*

Petitioner contends that claims 1–14 are unpatentable as obvious over the combination of Ma and Perrone. Pet. 47–59. The unavailability of Ma undermines Petitioner’s obviousness ground, which relies on Ma alone 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 that Petitioner establishes a reasonable likelihood of prevailing in showing that the subject matter of any challenged claim is unpatentable over Ma and Perrone.

IV. CONCLUSION

Petitioner has not established a reasonable likelihood of prevailing on its assertion that claims 1–14 are unpatentable.

V. ORDER

For the reasons given, it is:

ORDERED that the Petition is *denied* as to all challenged claims of the '580 patent and no trial is instituted.

IPR2018-00119  
Patent 7,964,580 B2

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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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INITIATIVE FOR MEDICINES, ACCESS & KNOWLEDGE (I-MAK), INC.,  
Petitioner,

v.

GILEAD PHARMASSET LLC,  
Patent Owner.

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IPR2018-00120  
Patent 7,964,580 B2

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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 1–14 of U.S. Patent No. 7,964,580 B2 (“the ’580 patent”). Paper 2 (“Pet.”). Gilead Pharmasset LLC (“Patent Owner”) filed a Preliminary Response. Paper 6 (“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 ’580 patent, IPR2018-00119. Pet. 2; Paper 4, 3. Patent Owner also identifies additional petitions filed by Petitioner for *inter partes* review of other patents owned by Patent Owner: IPR2018-00121 and IPR2018-00122 for U.S. Patent No. 8,334,270 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 '580 Patent (Ex. 1001)*

The '580 patent is directed to, *inter alia*, a phosphoramidate prodrug of a nucleoside derivative for treatment of viral infections in mammals, its ester, or a stereoisomer thereof. Ex. 1001, Abstract, 493:42–45. The '580 patent also addresses methods of treatment, uses, and processes for preparing such compounds. *Id.*, Abstract.

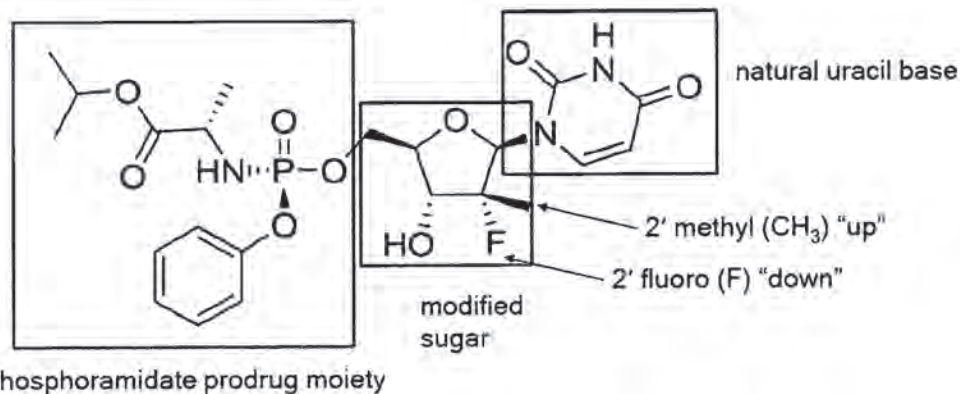
*C. Illustrative Claims*

Independent claims 1 and 8—reproduced below—are illustrative of the claimed subject matter.

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8. (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.

Ex. 1001, 493:42–45, 495:27–80.

Claim 8 is directed to the Sp stereoisomer (i.e., sofosbuvir), whereas claim 1 covers the Sp stereoisomer, the Rp stereoisomer, and mixtures of the two. Prelim. Resp. 3–4, 12; *see also* Pet. 28–29. The structure of sofosbuvir, as annotated by Patent Owner, is depicted below:



Prelim. Resp. at 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.*

*D. The Asserted Grounds of Unpatentability*

Petitioner asserts that claims 1–14 of the '580 patent are unpatentable based on the following grounds. Pet. 3.

| References                                                                 | Statutory Basis |
|----------------------------------------------------------------------------|-----------------|
| Clark '147, <sup>1</sup> Clark 2005, <sup>2</sup> and Perrone <sup>3</sup> | § 103           |
| Clark '147, Clark 2005, and McGuigan <sup>4</sup>                          | § 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,

<sup>1</sup> Clark, WO 2005/003147 A2, published January 13, 2005 (Ex. 1006).

<sup>2</sup> Clark et al., 48 J. MED. CHEM. 5504–08 (2005) (Ex. 1007).

<sup>3</sup> Perrone et al., 50 J. MED. CHEM. 1840–49 (2007) (Ex. 1008).

<sup>4</sup> McGuigan, WO 2005/012327 A2, published February 10, 2005 (Ex. 1009).

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

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*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 appear. 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 ‘580 [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)*

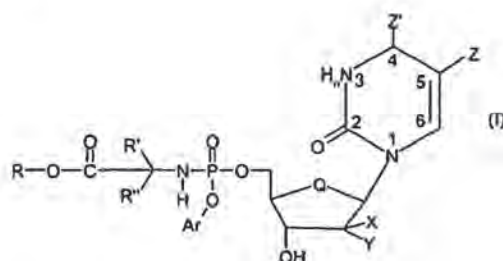
Perrone reports that “4’-[a]zidouridine did not inhibit HCV, although 4’-azidocytidine was a potent inhibitor of HCV replication under similar assay conditions” and that “4’-azidouridine triphosphate was a potent inhibitor of RNA synthesis by HCV polymerase.” Ex. 1008, 1. Perrone reports the synthesis 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,<sup>5</sup> 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.

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<sup>5</sup> Perrone states that “the phenyl substituent on the phosphate [of the phenyl phosphoramidates 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 1–14 are unpatentable as obvious over the combination of Clark '147, Clark 2005, and Perrone. Pet. 28–45.

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.*).

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-methyl cytidine 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 ¶ 174).

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 ¶ 175). 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 ¶ 177. 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 ¶ 179).

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 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 ¶ 184).

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 ¶ 195). 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-methyl

uridine as a practicable HCV inhibitor.” Pet. 34 (citing Ex. 1002 ¶ 175). 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 ¶ 177), 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). 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 ¶ 203.

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; Ex. 1002 ¶ 188. 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 ¶ 195.

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. 16–22), and contends that “it was generally known that, for antiviral 5'-phosphate prodrugs, the antiviral activity lies in the nucleoside itself” (*id.* at 18 (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 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. 19; 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. 19; 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. 17–18, 42 (citing Ex. 1012, 1, 4), 14–15, 17 (citing Ex. 1013, 3), 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'-2'-fluoro-2'-C-methyluridine resulting[, when the phosphoramidate of compound is used,] in the compounds of claims 1 and 8." *Id.* at 40 (citing Ex. 1002 ¶ 192; 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 ¶ 194; Ex. 1008, 3–4.

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 the claimed subject matter.

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. 13–17), some arguments are applicable to both theories (*id.* at 17–32).

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 the (phenyl)(isopropyl-L-alaninyl)phosphate. Prelim. Resp. 27–32. 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 28–29. Patent Owner further argues that Petitioner “offers no evidence . . . that a person of ordinary skill would disregard these structural differences.” *Id.* at 29 (citing Pet. 38–41; Ex. 1002 ¶¶ 18, [sic] 195).

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 29–30. 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. 29 (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 phosphoramidates with 2'-deoxy-2'-fluoro-2'-C-methyluridine would yield an anti-HCV drug that was both effective and non-toxic.” Prelim. Resp. 30. Patent Owner relies on the fact that “Perrone teaches that the most active compound prepared [compound 33], which was also nontoxic, was a 1-naphthyl[sic] substituted compound . . . [while] applying a 1-naphthyl[sic] substitution to a 2'-deoxy-2'-fluoro-2'-C-methyluridine nucleoside resulted in a toxic compound.”<sup>6</sup> *Id.* at 30–31 (citing Ex. 1008, 5; Ex. 2015 (Sofia 2010)). Patent Owner cites to the “report[] that ‘[a]lthough the 1-naphthol ester substitution produced the most potent HCV inhibitor, **this substitution also led to substantial cytotoxicity** and was therefore not considered a viable substituent.” *Id.* (quoting Ex. 2015, 4, with added emphasis). Sofia 2010

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<sup>6</sup> Patent Owner inadvertently refers to 4'-azidocytidine in stating that “applying a 1-naphthyl[sic] substitution to 4'-azidocytidine resulted in a non-toxic compound” (Prelim. Resp. 30) rather than 4'-azidouridine which was the parent nucleoside in each of compounds 11–35 (see, e.g., Ex. 1008, 5 (“Interestingly, application of similar ProTide methods to the active 4'-azidocytidine gave little or no boost in anti-HCV activity (data not shown)).”

reports, in particular, that compound 29, the compound with a 1-naphthol ester substitution, significantly inhibits cellular rRNA replication (95.4% inhibition) under conditions in which the corresponding phenyl ester, compound 12, does not inhibit cellular rRNA replication (0% inhibition). *Compare* Ex. 2015, 4, Table 2, with Table 1.

Patent Owner also argues that Petitioner “ignores that the most active phosphoramidate disclosed in Perrone is . . . naphthyl-substituted” and that “even if motivated to modify the 2'-deoxy-2'-fluoro-2'-C-methyluridine . . . one of ordinary skill would be directed towards” a naphthyl rather than phenyl ester at the phosphate and a benzyl rather than isopropyl ester of the amino acid moiety. Prelim. Resp. 32.

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 '580 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 ¶¶ 175, 179.

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 ¶ 195) and on the notion that the antiviral activity lies on the nucleoside itself (Pet. 18). 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. 29–31.

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. 10–18, 20–22, 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 phosphoramidates being finite, small, or easily traversed, even if the range of options were to be limited as Petitioner contends in stating that “the amino acid moiety is most often glycine, alanine or valine, . . . the ester on

the amino acid is most often methyl, isopropyl, or benzyl” and “[t]he useful ester groups on phosphorus are aryl (typically phenyl).” Pet. 19; Ex. 1002 ¶¶ 65–66; Ex. 1008.

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. In re 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

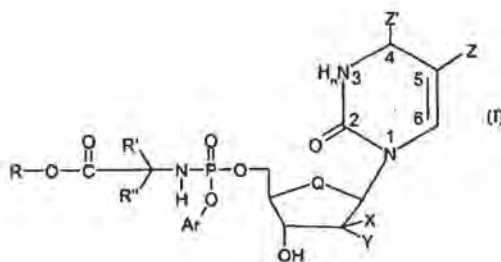
challenged claim is unpatentable over the combination of Clark '147, Clark 2005, and Perrone.

2. *Obviousness over Clark '147, Clark 2005, and McGuigan*

Petitioner contends that claims 1–14 are unpatentable as obvious over the combination of Clark '147, Clark 2005, and McGuigan. Pet. 45–61.

As set forth above, 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 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.

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 (-CH<sub>3</sub>)” for X and Y and that “Z’ is =O” rather than -NH<sub>2</sub>. Pet. 55–56; Ex. 1002 ¶ 229.

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” substituents such that “the compound of formula (I) of McGuigan . . . would be identical to the compound of claims 1 and 8.” Pet. 56 (citing Ex. 1002 ¶ 231). 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 ¶ 230.

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 ¶ 231).

Petitioner contends that “[t]hus, it would have been obvious to a person skilled in the art to obtain the compound of claims 1 and 8 based on Clark ‘147, Clark 2005 and McGuigan . . . in combination with the general knowledge in the art at the time.” *Id.* at 56–57; Ex. 1002 ¶ 232.

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. 37–38, *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 (-C<sub>4</sub>H<sub>9</sub>) or benzyl (-CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>)” (Ex. 1009, 9:20–21). Further, McGuigan states in “[t]he next sentence . . . that ‘[m]ost preferably, *R* is benzyl.’” Prelim. Resp. 37 (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*CF<sub>3</sub>CH<sub>6</sub>H<sub>4</sub>-, *p*NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>-, *p*ClC<sub>6</sub>H<sub>4</sub>- and *o*ClC<sub>6</sub>H<sub>4</sub>-.” Ex. 1009, 13:1–2; *see also* Prelim. Resp. 37–38. 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. 33–34), 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 ¶ 229). 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. 34).

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 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 1–14 are unpatentable.

#### V. ORDER

For the reasons given, it is:

ORDERED that the Petition is *denied* as to all challenged claims of the ’580 patent and no trial is instituted.

IPR2018-00120  
Patent 7,964,580 B2

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AO 120 (Rev. 08/10)

|     |                                                                                                                                                     |                                                                                                                         |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| TO: | <b>Mail Stop 8</b><br><b>Director of the U.S. Patent and Trademark</b><br><b>Office</b><br><b>P.O. Box 1450</b><br><b>Alexandria, VA 22313-1450</b> | <b>REPORT ON THE</b><br><b>FILING OR DETERMINATION OF AN</b><br><b>ACTION REGARDING A PATENT OR</b><br><b>TRADEMARK</b> |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|

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.<br>3:18-cv-04273-PGS-TJB | DATE FILED<br>3/27/2018 | U.S. DISTRICT COURT<br>TRENTON, NJ          |
| PLAINTIFF<br>GILEAD SCIENCES, INC.  |                         | DEFENDANT<br>TEVA PHARMACEUTICALS USA, INC. |

| PATENT OR<br>TRADEMARK NO. | DATE OF PATENT<br>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<br>_____ Amendment    _____ Answer    _____ Cross Bill    _____ Other Pleading |
| PATENT OR<br>TRADEMARK NO. | DATE OF PATENT<br>OR TRADEMARK                                                             |
| 1                          |                                                                                            |
| 2                          |                                                                                            |
| 3                          |                                                                                            |
| 4                          |                                                                                            |
| 5                          |                                                                                            |

In the above—entitled case, the following decision has been rendered or judgement issued:

|                    |
|--------------------|
| DECISION/JUDGEMENT |
|--------------------|

|                           |                                     |                   |
|---------------------------|-------------------------------------|-------------------|
| CLERK<br>William T. Walsh | (BY) DEPUTY CLERK<br>s/ John Moller | DATE<br>3/27/2018 |
|---------------------------|-------------------------------------|-------------------|

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)

|                                                                                                                                                         |                                                                                                                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| <b>TO:</b><br><b>Mail Stop 8</b><br><b>Director of the U.S. Patent and Trademark Office</b><br><b>P.O. Box 1450</b><br><b>Alexandria, VA 22313-1450</b> | <b>REPORT ON THE</b><br><b>FILING OR DETERMINATION OF AN</b><br><b>ACTION REGARDING A PATENT OR</b><br><b>TRADEMARK</b> |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|

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<br>_____ of Delaware                                            |
| PLAINTIFF<br>GILEAD SCIENCES, INC. and GILEAD PHARMASSET LLC |                             | DEFENDANT<br>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<br><input type="checkbox"/> Amendment <input type="checkbox"/> Answer <input type="checkbox"/> Cross Bill <input type="checkbox"/> Other Pleading |                               |
| PATENT OR TRADEMARK NO. | DATE OF PATENT OR TRADEMARK                                                                                                                                   | HOLDER 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 | (BY) DEPUTY CLERK | DATE |
|-------|-------------------|------|

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Copy 2—Upon filing document adding patent(s), mail this copy to Director Copy 4—Case file copy

| <b>PATENT OR<br/>TRADEMARK NO.</b> | <b>DATE OF PATENT OR<br/>TRADEMARK</b> | <b>HOLDER OF PATENT OR<br/>TRADEMARK</b> |
|------------------------------------|----------------------------------------|------------------------------------------|
| 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                    |