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(54) **3',5'-CYCLIC PHOSPHORAMIDATE  
PRODRUGS FOR HCV INFECTION**

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See application file for complete search history.

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

3,480,613 A 11/1969 Walton et al.  
6,174,868 B1 1/2001 Anderson et al.  
6,284,458 B1 9/2001 Anderson et al.  
6,348,587 B1 2/2002 Schinazi et al.  
6,391,542 B1 5/2002 Anderson et al.  
6,423,489 B1 7/2002 Anderson et al.  
6,433,159 B1 8/2002 Anderson  
6,455,513 B1 9/2002 McGuigan et al.  
6,566,365 B1 5/2003 Storer  
6,573,247 B1 6/2003 McGuigan et al.

6,608,191 B1 8/2003 Anderson et al.  
6,638,919 B2 10/2003 McGuigan et al.  
6,660,721 B2 12/2003 Devos et al.  
6,777,395 B2 8/2004 Bhat et al.  
6,784,161 B2 8/2004 Ismaili et al.  
6,784,166 B2 8/2004 Devos et al.  
6,833,361 B2 12/2004 Hong et al.  
6,846,810 B2 1/2005 Martin et al.  
6,911,424 B2 6/2005 Schinazi et al.  
6,914,054 B2 7/2005 Sommadossi et al.  
6,927,291 B2 8/2005 Jin et al.  
6,995,146 B2 2/2006 Anderson et al.  
7,018,989 B2 3/2006 McGuigan et al.  
7,019,135 B2 3/2006 McGuigan et al.  
7,094,770 B2 8/2006 Watanabe et al.  
7,105,493 B2 9/2006 Sommadossi et al.  
7,105,499 B2 9/2006 Carroll et al.  
7,115,590 B1 10/2006 Daluge et al.  
7,125,855 B2 10/2006 Bhat et al.  
7,138,376 B2 11/2006 Gosselin et al.  
7,148,206 B2 12/2006 Sommadossi et al.  
7,157,441 B2 1/2007 Sommadossi et al.  
7,163,929 B2 1/2007 Sommadossi et al.  
7,169,766 B2 1/2007 Sommadossi et al.  
7,192,936 B2 3/2007 LaColla et al.  
7,202,224 B2 4/2007 Eldrup et al.  
7,300,924 B2 11/2007 Boojamra et al.  
7,307,065 B2 12/2007 Schinazi et al.  
7,323,449 B2 1/2008 Olsen et al.  
7,323,453 B2 1/2008 Olsen et al.  
7,339,054 B2 3/2008 Xu et al.  
7,365,057 B2 4/2008 LaColla et al.

(Continued)

**FOREIGN PATENT DOCUMENTS**

CN 1133642 C 1/2004  
CN 103848876 A 6/2014

(Continued)

**OTHER PUBLICATIONS**

Silverman et al., *The Organic Chemistry of Drug Design and Drug  
Action*, pp. 19-23, 1992.\*

International Search Report and Written Opinion in PCT/US2013/  
042058, mailed Jul. 11, 2013, 12 pages.

Congiatu et al., "Novel Potential Anticancer Naphthyl  
Phosphoramidates of BVdU: Separation of Diastereoisomers and  
Assignment of the Absolute Configuration of the Phosphorus Center"  
*Journal of Medicinal Chemistry* 49:452-455 (2006).

Eldrup et al., Structure-Activity Relationship of Purine  
Ribonucleosides for Inhibition of Hepatitis C Virus RNA-Dependent  
RNA Polymerase *J. Med. Chem.* 47:2283-2295 (2004).

(Continued)

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(57)

**ABSTRACT**

Provided herein are compounds, compositions and methods  
for the treatment of Flaviviridae infections, including HCV  
infections. In certain embodiments, compounds and compo-  
sitions of nucleoside derivatives are disclosed, which can be  
administered either alone or in combination with other anti-  
viral agents.

**28 Claims, No Drawings**