



US009186369B2

(12) **United States Patent**
Storer et al.

(10) **Patent No.:** **US 9,186,369 B2**
(45) **Date of Patent:** **Nov. 17, 2015**

(54) **PURINE NUCLEOSIDE ANALOGUES FOR TREATING FLAVIVIRIDAE INCLUDING HEPATITIS C**

(71) Applicants: **Idenix Pharmaceuticals, Inc.**, Cambridge, MA (US); **The Centre National de la Recherche Scientifique**, Paris-Cedex (FR); **L'Universite Montpellier II**, Montpellier (FR)

(72) Inventors: **Richard Storer**, Folkestone (GB); **Gilles Gosselin**, Montpellier (FR); **David Dukhan**, Montpellier (FR); **Frederic Leroy**, Jonquieres (FR)

(73) Assignee: **Idenix Pharmaceuticals, LLC**, Cambridge, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/269,003**

(22) Filed: **May 2, 2014**

(65) **Prior Publication Data**

US 2014/0234251 A1 Aug. 21, 2014

Related U.S. Application Data

(60) Division of application No. 12/270,795, filed on Nov. 13, 2008, now Pat. No. 8,742,101, which is a continuation of application No. 10/900,008, filed on Jul. 26, 2004, now abandoned.

(60) Provisional application No. 60/490,216, filed on Jul. 25, 2003.

(51) **Int. Cl.**

C07H 19/23 (2006.01)
C07D 487/04 (2006.01)
C07D 405/04 (2006.01)
C07D 409/04 (2006.01)
A61K 31/7052 (2006.01)
A61K 31/5025 (2006.01)
A61K 31/53 (2006.01)
A61P 31/14 (2006.01)
A61K 31/706 (2006.01)
A61K 31/00 (2006.01)
C07H 19/044 (2006.01)
C07H 19/052 (2006.01)
C07H 19/056 (2006.01)
A61K 45/06 (2006.01)
C07H 19/04 (2006.01)

(52) **U.S. Cl.**

CPC **A61K 31/706** (2013.01); **A61K 31/00** (2013.01); **A61K 45/06** (2013.01); **C07H 19/04** (2013.01); **C07H 19/044** (2013.01); **C07H 19/052** (2013.01); **C07H 19/056** (2013.01); **C07H 19/23** (2013.01)

(58) **Field of Classification Search**

CPC C07H 19/23; C07H 19/12; C07D 487/04; C07D 405/04; C07D 409/04; A61K 31/7052; A61K 31/5025; A61K 31/53; A61K 45/06
USPC 536/27.13; 514/43, 45, 48; 544/236
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,798,209 A 3/1974 Witkowski et al.
RE29,835 E 11/1978 Witkowski et al.
4,211,771 A 7/1980 Witkowski et al.
4,522,811 A 6/1985 Eppstein et al.
5,026,687 A 6/1991 Yarchoan et al.
5,055,394 A 10/1991 Kopecko et al.
5,149,794 A 9/1992 Yatvin et al.
5,194,654 A 3/1993 Hostetler et al.
5,223,263 A 6/1993 Hostetler et al.
5,372,808 A 12/1994 Blatt et al.
5,496,546 A 3/1996 Wang et al.
5,538,865 A 7/1996 Reyes et al.
5,610,054 A 3/1997 Draper
5,633,358 A 5/1997 Gruetzke et al.
5,676,942 A 10/1997 Testa et al.
5,725,859 A 3/1998 Omer
5,738,845 A 4/1998 Imakawa
5,830,455 A 11/1998 Valtuena et al.
5,837,257 A 11/1998 Tsai et al.
5,846,964 A 12/1998 Ozeki
5,849,696 A 12/1998 Chretien et al.
5,869,253 A 2/1999 Draper

(Continued)

FOREIGN PATENT DOCUMENTS

DE 19914474 10/1999
EP 0350287 1/1990

(Continued)

OTHER PUBLICATIONS

Bussolari et al. *J. Med. Chem.* 1993, 36(25) 4113-4120.*
Meade et al. *J. Med. Chem.* 1992, 35(3) 526-533.*
Acedo et al., "Synthesis and Biophysical and Biological Properties of Oligonucleotides Containing 2-Aza-2'-Deoxyinosine," *J. Org. Chem.* 1995, vol. 60, pp. 6262-6269.
Alt et al., "Core specific antisense phosphorothioate oligodeoxynucleotides as potent and specific inhibitors of hepatitis C viral translation," *Arch. Virol.* 1997, vol. 142, pp. 589-599.

(Continued)

Primary Examiner — Venkataraman Balasubramanian

(74) *Attorney, Agent, or Firm* — Jones Day

(57) **ABSTRACT**

This invention is directed to a method for treating a host, especially a human, infected with hepatitis C, flavivirus and/or pestivirus, comprising administering to that host an effective amount of an anti-HCV biologically active pentofuranonucleoside where the pentofuranonucleoside base is an optionally substituted 2-azapurine. The optionally substituted pentofuranonucleoside, or a salt or prodrug thereof, may be administered alone or in combination with one or more optionally substituted pentofuranonucleosides or other anti-viral agents.

28 Claims, 3 Drawing Sheets