

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
31 January 2002 (31.01.2002)

PCT

(10) International Publication Number
WO 02/008241 A3

(51) International Patent Classification⁷: **C07F 9/6561**,
C07H 19/20, G01N 33/53, A61K 31/675, A61P 31/12,
35/00

ROHLOFF, John, C. [US/US]; 1654 Cornell Drive,
Mountain View, CA 94040 (US). **SPARACINO, Mark,
L.** [US/US]; 1450 Seville Drive, Morgan Hill, CA 95037
(US).

(21) International Application Number: PCT/US01/23104

(74) Agents: **HENSLEY, Max, D.** et al.; Gilead Sciences, Inc.,
333 Lakeside Drive, Foster City, CA 94404 (US).

(22) International Filing Date: 20 July 2001 (20.07.2001)

(25) Filing Language: English

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
ZW.

(26) Publication Language: English

(30) Priority Data:
60/220,021 21 July 2000 (21.07.2000) US

(63) Related by continuation (CON) or continuation-in-part
(CIP) to earlier application:
US 60/220,021 (CIP)
Filed on 21 July 2000 (21.07.2000)

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG).

(71) Applicant (*for all designated States except US*): **GILEAD
SCIENCES, INC.** [US/US]; 333 Lakeside Drive, Foster
City, CA 94404 (US).

(72) Inventors; and

Published:

— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

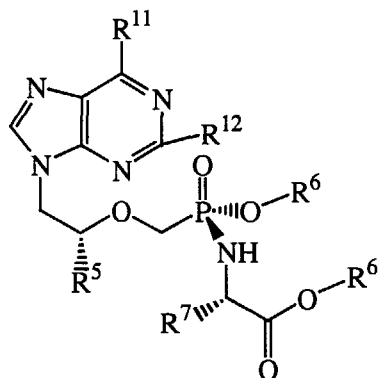
(75) Inventors/Applicants (*for US only*): **BECKER, Mark,
W.** [US/US]; 215 Old County Road #308, Belmont, CA
94002 (US). **CHAPMAN, Harlan, H.** [US/US]; 60 La-
guna Drive, La Honda, CA 94020 (US). **CIHLAR, Tomas**
[CZ/US]; 727 Caravel Lane, Foster City, CA 94404 (US).
EISENBERG, Eugene, J. [US/US]; 236 Club Drive, San
Carlos, CA 94070 (US). **HE, Gong-Xin** [CN/US]; 5436
Ontario Common, Fremont, CA 94555 (US). **KERNAN,
Michael, R.** [US/US]; 6 Sequoia Way, Pacifica, CA 94044
(US). **LEE, William, A.** [US/US]; 749 Anderson Drive,
Los Altos, CA 94024 (US). **PRISBE, Ernest, J.** [US/US];
1336 Richardson Avenue, Los Altos, CA 94024 (US).

(88) Date of publication of the international search report:
29 August 2002

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: PRODRUGS OF PHOSPHONATE NUCLEOTIDE ANALOGUES AND METHODS FOR SELECTING AND MAK-
ING SAME

WO 02/008241 A3



(5a)

(57) Abstract: A novel method is provided for screening prodrugs of methoxyphosphonate nucleotide analogues to identify prodrugs selectively targeting desired tissues with antiviral or antitumor activity. This method has led to the identification of novel mixed ester-amidates of PMPA for retroviral or hepadnaviral therapy, including compounds of structure (5a) having substituent groups as defined herein. Compositions of these novel compounds in pharmaceutically acceptable excipients and their use in therapy and prophylaxis are provided. Also provided is an improved method for the use of magnesium alkoxide for the preparation of starting materials and compounds for use herein.