

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 May 2008 (08.05.2008)

PCT

(10) International Publication Number
WO 2008/055068 A3

(51) International Patent Classification:

C07D 209/22 (2006.01) A61K 31/5513 (2006.01)
C07D 209/70 (2006.01) A61P 43/00 (2006.01)
C07D 221/12 (2006.01) C07D 239/34 (2006.01)
C07D 223/26 (2006.01) C07D 239/42 (2006.01)
C07D 225/08 (2006.01) C07D 243/14 (2006.01)
C07D 239/28 (2006.01) C07D 243/24 (2006.01)
A61K 31/55 (2006.01) A61K 31/553 (2006.01)
A61K 31/554 (2006.01)

Kingston Street, Unit 5f, Boston, MA 02111 (US). SMIL, David [CA/CA]; #907-380 Rive Boisee, Montreal, Qc, H8Z 3K4 (CA).

(74) Agent: GREENFIELD, Michael, S.; McDonnell Boehnen Hulbert & Berghoff LLP, 300 South Wacker Drive, Suite 3100, Chicago, IL 60606 (US).

(21) International Application Number:

PCT/US2007/082668

(22) International Filing Date: 26 October 2007 (26.10.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/863,347 28 October 2006 (28.10.2006) US
60/884,287 10 January 2007 (10.01.2007) US

(71) Applicants (for all designated States except US): METHYGENE INC. [CA/CA]; 7220 Frederick-banting, Montreal, QCH4S 2A1 (CA). EN VIVO PHARMACEUTICALS, INC. [US/US]; 480 Arsenal Street, Building 1, Watertown, MA 02472 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): DEZIEL, Robert [CA/CA]; 546 Chester Avenue, Mount-royal, QC H3R 1W9 (CA). LEIT, Silvana [CA/CA]; 27 Rolland-laniel, Kirkland, QC H9J 4A5 (CA). BEAULIEU, Patrick [CA/CA]; 724, Place De Monaco, Apt. 87, Laval, QC H7N 6G3 (CA). CHANTIGNY, Yves, Andre [CA/CA]; 212 Champlain, Pincourt, QC J7V 5E6 (CA). MANCUSO, John [CA/CA]; 500 Valois St. Unit 4, Vaudreuil, QC J7V IT4 (CA). TESSIER, Pierre [CA/CA]; 491 Wolfe Street, Hawkesbury, ON K6A 1V8 (CA). SHAPIRO, Gideon [US/US]; 5507 Nw 80th Avenue, Gainesville, FL 32653 (US). CHESWORTH, Richard [GB/US]; 88

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

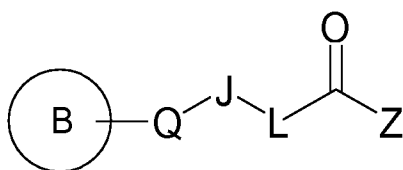
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
5 March 2009

(15) Information about Correction:

Previous Correction:
see Notice of 24 July 2008

(54) Title: INHIBITORS OF HISTONE DEACETYLASE



(I)

(57) Abstract: This invention relates to compounds for the inhibition of histone deacetylase. More particularly, the invention provides for compounds of formula (I) wherein (B), Q, J, L and Z are as defined in the specification.



WO 2008/055068 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/082668

A. CLASSIFICATION OF SUBJECT MATTER					
INV.	C07D209/22	C07D209/70	C07D221/12	C07D223/26	C07D225/08
	C07D239/28	A61K31/55	A61K31/554	A61K31/5513	A61P43/00
	C07D239/34	C07D239/42	C07D243/14	C07D243/24	A61K31/553

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D A61K A61P

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

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

EPO-Internal, WPI Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MILLER T A: "Patent status of histone deacetylase inhibitors" EXPERT OPINION ON THERAPEUTIC PATENTS, ASHLEY PUBLICATIONS, GB, vol. 14, no. 6, 1 January 2004 (2004-01-01), pages 791-804, XP002294154 ISSN: 1354-3776 paragraph [0003]; compounds 1-30A	1-98
X	WO 2006/097449 A (MENARINI INTERNAT OPERATIONS L [LU]; GUIDI ANTONIO [IT]; DIMOULAS TULA) 21 September 2006 (2006-09-21) page 1, line 5 - page 2, line 30; claim 1; example 1; compound (I)	1-98

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

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

"E" earlier document but published on or after the international filing date

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 September 2008	15/01/2009
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Moriggi, J

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/082668

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/076401 A (JANSSEN PHARMACEUTICA NV [BE]; EMELN KRISTOF VAN [BE]; BACKX LEO JACO) 18 September 2003 (2003-09-18) page 1, line 5 - line 9; claim 1; compounds 25,28 -----	1-98
X	WO 02/085883 A (HOFFMANN LA ROCHE [CH]) 31 October 2002 (2002-10-31) page 1, line 1 - line 8; claim 1; examples 2-7 -----	1,2, 6-18,20, 21, 23-41, 46-48, 72,73, 75-79, 81-89, 92-98
X	EP 0 030 254 A (SCHERING AG [DE]; FERROSAN AS [DK]) 17 June 1981 (1981-06-17) page 40; table III; compound 8TH -----	1,2, 6-18,20, 21, 23-41, 46-48, 72,73, 75-79, 81-89, 92-98

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/082668

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

part of claims 1, 2, 6-18, 20, 21, 23-41, 46-48, 72, 73, 75-79, 81-89
92-98

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: part of claims 1, 2, 6-18, 20, 21, 23-41, 46-48, 72, 73, 75-79, 81-89, 92-98

the compounds of formula (I) of claim 1, wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B is a ring system made of only three fused rings that are a 6-membered ring fused to a 5-membered ring fused to a 6-membered ring

2. claims: part of claims 1, 2, 6-18, 20, 21, 23-28, 30-41, 46-48, 72, 73, 75-79, 81-89, 92-98

the compounds of formula (I) of claim 1 wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B is a ring system made of only three fused rings that are a 6-membered ring fused to a 6-membered ring fused to a 6-membered ring

3. claims: 45 and 66-70, as well as part of claims 1-21, 23-44, 46-48, 52-65, 71-73, 75-79, 81-89, 92-98

the compounds of formula (I) of claim 1 wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B is a ring system made of only three fused rings that are a 6-membered ring fused to a 7-membered ring fused to a 6-membered ring

4. claims: part of claims 1, 2, 6-18, 20, 21, 23-28, 30-41, 47, 48, 52-65, 72, 73, 75-79, 81-84, 92-98

the compounds of formula (I) of claim 1 wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B is a ring system made of only three fused rings that are a 5-membered ring fused to a 7-membered ring fused to a 5-membered ring

5. claims: part of claims 1, 2, 6-18, 20, 21, 23-28, 30-41, 47-48, 52-65, 71-73, 75-79, 81-84, 89, 92-98

the compounds of formula (I) of claim 1 wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B is a ring system made of only three fused rings that are a 5- or a 7-membered ring fused to respectively a 7- or 5-membered ring fused to a 6-membered ring

6. claims: part of claims 1, 2, 6-18, 20, 21, 23-28, 30-41, 47-48, 72, 73, 75-79, 81-84, 92-98

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

the compounds of formula (I) of claim 1 wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B is a ring system made of only three fused rings that are a 5-membered ring fused to a 6-membered ring fused to a 6-membered ring or a 6-membered ring fused to a 5-membered ring fused to a 5-membered ring

7. claims: part of claims 1, 2, 6-18, 20, 21, 23-42, 44, 46-48, 72, 73, 75-79, 81-89, 92-98

the compounds of formula (I) of claim 1 wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B is a ring system made of three fused rings containing at least one 8-membered ring

8. claims: 49-51 and part of claims 1, 2, 4, 6-18, 20, 21, 23-48, 72, 73, 75-84, 86, 88, 92-98

the compounds of formula (I) of claim 1 wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B contains less than 3 fused rings (including monocycles, i.e. non-fused rings)

9. claims: part of claims 1, 2, 6-18, 20, 21, 23-28, 30-41, 47, 48, 71-73, 75-79, 81-84, 92-98

the compounds of formula (I) of claim 1 wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B contains more than 3 fused rings

10. claims: part of claims 1, 6-18, 20, 21, 23-28, 30-35, 38-41, 92-98

the compounds of formula (I) of claim 1, wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B is absent

11. claims: part of claims 1, 6-18, 20, 21, 23-28, 30-36, 38-41, 72, 73, 75-84, 92-98

the compounds of formula (I) of claim 1, wherein -L-C(O)-Z is -C(O)N(R1)OR2 and B is hydrogen or C1-C10alkyl

12. claims: 22, 74 and 90, as well as part of claims 1-9, 18, 19, 23-41, 43, 44, 46, 52, 53, 72, 75-80, 92-98

the compounds of formula (I) of claim 1, wherein -L-C(O)-Z is -N(OR2)-CHO

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2007/082668

Patent document cited in search report	A	Publication date		Patent family member(s)	Publication date
WO 2006097449	A	21-09-2006		AR 053171 A1	25-04-2007
				AU 2006222883 A1	21-09-2006
				CA 2600521 A1	21-09-2006
				CN 101142197 A	12-03-2008
				EP 1863776 A1	12-12-2007
				JP 2008533088 T	21-08-2008
				KR 20080003336 A	07-01-2008
				US 2008275023 A1	06-11-2008
WO 03076401	A	18-09-2003		AU 2003209727 A1	22-09-2003
				CA 2476186 A1	18-09-2003
				DK 1485354 T3	01-09-2008
				EP 1485354 A1	15-12-2004
				ES 2306880 T3	16-11-2008
				HR 20040801 A2	30-04-2005
				JP 2005526763 T	08-09-2005
				MX PA04007776 A	15-10-2004
WO 02085883	A	31-10-2002		AT 306480 T	15-10-2005
				BR 0209064 A	10-08-2004
				CA 2442994 A1	31-10-2002
				CN 1507441 A	23-06-2004
				DE 60206616 T2	13-07-2006
				EP 1385837 A1	04-02-2004
				ES 2249572 T3	01-04-2006
				JP 4142453 B2	03-09-2008
				JP 2005503341 T	03-02-2005
				MX PA03009132 A	12-02-2004
				US 2002183513 A1	05-12-2002
				ZA 200307793 A	06-01-2005
EP 0030254	A	17-06-1981		CA 1150246 A1	19-07-1983
				DD 152935 A5	16-12-1981
				ES 8106305 A1	16-10-1981
				FI 802720 A	01-03-1981
				HU 186744 B	30-09-1985
				IE 50229 B1	05-03-1986
				IL 60906 A	29-11-1985
				NO 802546 A	02-03-1981
				NZ 194747 A	29-11-1988
				PL 226479 A1	30-10-1981
				PT 71744 A	01-09-1980
				RO 80265 A1	29-04-1983
				US 4371536 A	01-02-1983
				US 5010077 A	23-04-1991
	YU 215580 A1	29-02-1984			