



(51) International Patent Classification:

C07D 251/22 (2006.01) C07D 405/14 (2006.01)
C07D 239/49 (2006.01) C07D 407/12 (2006.01)
C07D 401/12 (2006.01) C07D 407/14 (2006.01)
C07D 401/14 (2006.01) A61K 31/53 (2006.01)
C07D 403/12 (2006.01) A61K 31/505 (2006.01)
C07D 403/14 (2006.01) A61K 31/506 (2006.01)
C07D 405/12 (2006.01) A61P 35/00 (2006.01)

(21) International Application Number:

PCT/CN2013/079200

(22) International Filing Date:

11 July 2013 (11.07.2013)

(25) Filing Language:

English

(26) Publication Language:

English

(71) Applicant: AGIOS PHARMACEUTICALS, INC.
[US/US]; 38 Sidney Street, Cambridge, Massachusetts
02139 (US).

(72) Inventors: POPOVICI-MULLER, Janeta; 12 Clarke
Farm Rd., Windham, New Hampshire 03087 (US). CAI,
Zhenwei; 36 Hills Drive, Belle Mead, New Jersey 08502
(US). ZHOU, Ding; 52 Yishashi Garden, 188 Chunjiu
RD., Shanghai 201612 (CN).

(74) Agent: NTD PATENT AND TRADEMARK AGENCY
LIMITED; 10th Floor, Block A, Investment Plaza, 27 Jin-
rongdajie, Xicheng District, Beijing 100033 (CN).

(81) Designated States (unless otherwise indicated, for every

kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, 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, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, 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, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

12 March 2015

(54) Title: THERAPEUTICALLY ACTIVE COMPOUNDS AND THEIR METHODS OF USE

(57) Abstract: Provided are compounds useful for treating cancer and methods of treating cancer comprising administering to a sub-
ject in need thereof a compound described herein.



WO 2015/003360 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2013/079200

A. CLASSIFICATION OF SUBJECT MATTER

C07D251/22 (2006.01) i; C07D239/49 (2006.01) i; C07D401/12 (2006.01) i; C07D401/14 (2006.01) i; C07D403/12 (2006.01) i; C07D403/14 (2006.01) i; C07D405/12 (2006.01) i; C07D405/14 (2006.01) i; C07D407/12 (2006.01) i; C07D407/14 (2006.01) i; A61K31/53 (2006.01) i; A61K31/505 (2006.01) i; A61K31/506 (2006.01) i; A61P35/00 (2006.01) i

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)

C07D251/-; C07D239/-; C07D401/-; C07D403/-; C07D405/-; C07D407/-; A61K31/5+; A61P35/-

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 practicable, search terms used)

WPI; EPODOC; CNPAT; CNKI; CA ON CD; CAPLUS; REGISTRY(structure search): +triazin+, +pyrimidin+, +diazin+, +tumor+, +cancer+, +IDH+

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CN 102659765 A (UNIV SHENYANG PHARM) 12 September 2012 (2012-09-12) compounds of examples 39, 41, 43, 45-47, claims 1-11	1-3
X	GEWALD Rainer et al. "Discovery of triazines as potent, selective and orally active PDE4 inhibitors, " <i>Bioorganic & Medicinal Chemistry Letters</i> , No. Vol. 23, 31 December 2013 (2013-12-31), pp 4308-4314, Scheme 1, compound 21, compounds 35-36 of table 3, compounds 34, 37-47 of table 4, compound of Fig. 4	1-2
X	MORENO Karlos X. et al. "Identification of diamine linkers with differing reactivity and their application in the synthesis of melamine dendrimers, " <i>Tetrahedron Letters</i> , , No. Vol. 49, 31 December 2008 (2008-12-31), pp 1152-1154, compound 6 of Scheme 2, compound 1 of Scheme 4	1-2
X	BHUSHAN Ravi et al. "Reversed-phase liquid chromatographic resolution of diastereomers of protein and non-protein amino acids prepared with newly synthesized chiral derivatizing reagents based on cyanuric chloride, " <i>Amino Acids</i> , No. Vol. 40, 31 December 2011 (2011-12-31), pp 403-409, compounds of Fig. 1	1-2

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	“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
“E” earlier application or patent but published on or after the international filing date	“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
“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)	“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
“O” document referring to an oral disclosure, use, exhibition or other means	“&” document member of the same patent family
“P” document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

14 March 2014

Date of mailing of the international search report

12 January 2015

Name and mailing address of the ISA/CN

STATE INTELLECTUAL PROPERTY OFFICE OF THE
P.R.CHINA(ISA/CN)
6,Xitucheng Rd., Jimen Bridge, Haidian District, Beijing
100088 China

Authorized officer

HE,Xiaoping

Facsimile No. (86-10)62019451

Telephone No. (86-10)62084365

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MORENO Karlos et al. "Molecular recognition in dendrimers based on melamine, " <i>Polymer Preprints</i> , Vol. 2, No. 46, 31 December 2005 (2005-12-31), page 1127, compounds of Chart 2 and Scheme 1	1-2
X	LEE Jae Wook et al. "Combinatorial Solid-Phase Synthesis of 6-Aryl-1, 3, 5-triazines via Suzuki Coupling, " <i>Aust. J. Chem.</i> , No. Vol. 64, 31 December 2011 (2011-12-31), pp 540-544, compounds of Chart 1 and Scheme 1	1-2
X	DUANMU Chuansong et al. "Dendron-Functionalized Superparamagnetic Nanoparticles with Switchable Solubility in Organic and Aqueous Media: Matrices for Homogeneous, Catalysis and Potential MRI Contrast Agents, " <i>Chem. Mater.</i> , No. Vol. 18, 31 December 2006 (2006-12-31), pp 5973-5981, compound of Schemes 2-3 and Fig. 1	1-2
X	CHEN Hui-Ting et al. "Cytotoxicity, Hemolysis, and Acute in Vivo Toxicity of Dendrimers Based on Melamine, Candidate Vehicles for Drug Delivery, " <i>J. AM. CHEM. SOC.</i> , No. Vol. 126, 31 December 2004 (2004-12-31), pp 10044-10048, compounds of table 1	1-2
X	CN 102030918 A (FUJI FILM CO LTD) 27 April 2011 (2011-04-27) compounds 3-16, 4-3-4-10, 4-13-4-20, 4-24-4-30, 4-34-4-40, 4-43-4-50, 4-54-4-60, 4-64-4-70, 4-74-4-80, 4-84-90, 4-94-4-100, 4-104-4-110, 4-114-4-120	1-2
X	JP 4753336 B2 (NIPPON KAYAKU KK) 24 August 2011 (2011-08-24) compound 3	1-2
X	US 4084053 A (CIBA GEIGY CORP) 11 April 1978 (1978-04-11) compounds of columns 5-6, compounds in examples 2, 5 and 8	1-2
X	JP 08311047 A (NISSAN CHEMICAL IND LTD) 26 November 1996 (1996-11-26) compound 6	1-2
X	WO 2012074999 A1 (GALLEON PHARMACEUTICALS INC ET AL.) 07 June 2012 (2012-06-07) compound of example 26, 4th compound of table 7 of description	1-2
X	JP 11158073 A (TAKEDA CHEMICAL INDUSTRIES LTD) 15 June 1999 (1999-06-15) ref. compounds 23-35 and 44	1-2
X	WO 03016289 A1 (CIBA SC HOLDING AG ET AL.) 27 February 2003 (2003-02-27) table 1, compounds of examples 1-4, 6, 8	1-2
X	JP 2010181540 A (FUJI XEROX CO LTD) 19 August 2010 (2010-08-19) compounds A-13-A42, pages 16-18 of description	1-2
X	JP 2010079130 A (FUJI XEROX CO LTD) 08 April 2010 (2010-04-08) compounds A-13-A42, pages 18-20 of description	1-2
X	JP 2004107220 A (MITSUBISHI PHARMA CORP) 08 April 2004 (2004-04-08) compounds 23-24	1-2
X	JP 2009237115 A (FUJI XEROX CO LTD) 15 October 2009 (2009-10-15) compounds A13-15, 17, 21-22 on page 31 of description	1-2

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/CN2013/079200

Patent document cited in search report			Publication date (day/month/year)	Patent family member(s)			Publication date (day/month/year)
JP	2004107220	A	08 April 2004	Non e			
JP	2009237115	A	15 October 2009	JP	5277685	B2	28 August 2013
CN	102030918	A	27 April 2011	US	2011073007	A1	31 March 2011
				JP	5473851	B2	16 April 2014
				US	8465673	B2	18 June 2013
				JP	2011094120	A	12 May 2011
				CN	102030918	B	25 June 2014
JP	4753336	B2	24 August 2011	JP	2003073363	A	12 March 2003
US	4084053	A	11 April 1978	FR	2275476	B1	22 July 1977
				DE	2527288	A1	08 January 1976
				FR	2275476	A1	16 January 1976
				JP	S5114928	A	05 February 1976
				CH	606334	A5	31 October 1978
JP	08311047	A	26 November 1996	WO	9821191	A1	22 May 1998
				JP	H08311047	A	26 November 1996
CN	102659765	A	12 September 2012	CN	102659765	B	10 September 2014
WO	2012074999	A1	07 June 2012	EP	2646423	A1	09 October 2013
				CN	103347866	A	09 October 2013
				KR	20140049961	A	28 April 2014
				AU	2011336764	A1	20 June 2013
				US	2012142647	A1	07 June 2012
				EP	2646423	A4	30 April 2014
				SG	190921	A1	31 July 2013
				CA	2819333	A1	07 June 2012
				JP	2013544285	A	12 December 2013
JP	11158073	A	15 June 1999	JP	H11158073	A	15 June 1999
WO	03016289	A1	27 February 2003	JP	2005501855	A	20 January 2005
				AT	485281	T	15 November 2010
				JP	4344241	B2	14 October 2009
				US	2004242579	A1	02 December 2004
				DK	1423371	T3	07 February 2011
				US	7038046	B2	02 May 2006
				DE	60238066	D1	02 December 2010
JP	2010181540	A	19 August 2010	Non e			
JP	2010079130	A	08 April 2010	Non e			