US009409890B2

(12) **United States Patent**
van Duzer et al.

(10) **Patent No.: US 9,409,890 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **PYRIMIDINE HYDROXY AMIDE COMPOUNDS AS PROTEIN DEACETYLASE INHIBITORS AND METHODS OF USE THEREOF**

(71) Applicant: **Acetylon Pharmaceuticals, Inc.**, Boston, MA (US)

(72) Inventors: **John H. van Duzer**, Georgetown, MA (US); **Ralph Mazitschek**, Belmont, MA (US); **Yanbing Ding**, Richmond (CA); **Nan Yu**, Shanghai (CN); **Yun Cao**, Shanghai (CN); **Yong Liu**, Shanghai (CN)

(73) Assignee: **ACETYLON PHARAMCEUTICALS, INC.**, Boston, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 17 days.

(21) Appl. No.: **14/082,472**

(22) Filed: **Nov. 18, 2013**

(65) **Prior Publication Data**

US 2014/0142104 A1 May 22, 2014

Related U.S. Application Data

(63) Continuation of application No. 13/296,748, filed on Nov. 15, 2011, now Pat. No. 8,614,223.

(60) Provisional application No. 61/414,158, filed on Nov. 16, 2010, provisional application No. 61/503,286, filed on Jun. 30, 2011.

(51) **Int. Cl.**

A61K 31/505	(2006.01)
A61K 31/506	(2006.01)
C07D 239/42	(2006.01)
C07D 405/12	(2006.01)
C07D 401/12	(2006.01)
C07D 401/14	(2006.01)
C07D 403/12	(2006.01)
C07D 409/12	(2006.01)

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

CPC ***C07D 409/12*** (2013.01); ***C07D 239/42*** (2013.01); ***C07D 401/12*** (2013.01); ***C07D 401/14*** (2013.01); ***C07D 403/12*** (2013.01); ***C07D 405/12*** (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,549,633	A	12/1970	Grabowski et al.
6,777,217	B1	8/2004	Schreiber et al.
7,244,853	B2	7/2007	Schreiber et al.
7,250,504	B2	7/2007	Grozinger et al.
7,994,362	B2	8/2011	Schreiber et al.
8,148,526	B1	4/2012	van Duzer et al.
8,394,810	B2	3/2013	van Duzer et al.
8,609,678	B2	12/2013	van Duzer et al.
8,614,223	B2	12/2013	van Duzer et al.
9,145,412	B2	9/2015	van Duzer et al.
2004/0266769	A1	12/2004	Bressi
2006/0239909	A1	10/2006	Anderson
2007/0093413	A1	4/2007	Schreiber
2007/0149495	A1	6/2007	Bressi
2008/0207590	A1	8/2008	Deziel et al.
2009/0023786	A1	1/2009	Miller
2009/0209590	A1	8/2009	Mazitschek
2009/0305384	A1	12/2009	Grozinger
2009/0312363	A1	12/2009	Bradner
2010/0137196	A1	6/2010	Schreiber
2011/0218154	A1	9/2011	Schreiber
2011/0300134	A1	12/2011	van Duzer et al.
2013/0225543	A1*	8/2013	Jones et al. 514/171
2014/0011767	A1	1/2014	Yang et al.
2014/0142104	A1	5/2014	van Duzer et al.
2014/0142117	A1	5/2014	van Duzer et al.
2014/0243345	A1	8/2014	van Duzer et al.
2014/0249148	A1	9/2014	van Duzer et al.
2014/0357512	A1	12/2014	Jones et al.
2015/0045380	A1	2/2015	van Duzer et al.
2015/0099744	A1	4/2015	Yang et al.
2015/0105358	A1	4/2015	Quayle et al.
2015/0105383	A1	4/2015	Quayle et al.
2015/0105384	A1	4/2015	Jones et al.
2015/0105409	A1	4/2015	Quayle et al.
2015/0150871	A1	6/2015	Quayle et al.

FOREIGN PATENT DOCUMENTS

EP	2524918	A1	11/2012
WO	WO 03/037869	A1	5/2003
WO	03-076401	A1	9/2003
WO	WO03/076430	A1	9/2003
WO	WO 2004/052869	A1	6/2004
WO	WO 2005/012261	A1	2/2005
WO	WO 2006/102557	A2	9/2006
WO	WO 2006/123121	A1	11/2006
WO	WO 2007/022638	A1	3/2007
WO	WO 2007/091703	A1	8/2007
WO	WO 2007/130429	A2	11/2007
WO	WO 2008/055068	A2	5/2008
WO	WO 2008/091349	A1	7/2008
WO	2009/137503	A1	11/2009

(Continued)

OTHER PUBLICATIONS

Cancer Drug Design and Discovery, Neidle, Stephen ed. (Elsevier/Academic Press), pp. 427-431 (2008).*

Carey et al. Current Opinion in Pharmacology, vol. 6, p. 369-375 (2006).*

Lane et al.J.Clin.Oncol. 27, pp. 5459-5468 (2009).*

(Continued)

Primary Examiner — Emily Bernhardt

(74) *Attorney, Agent, or Firm* — Lathrop & Gage LLP; Brian C. Trinque

(57) **ABSTRACT**

The present invention relates to novel pyrimidine hydroxy amide compounds, and the use of such compounds in the inhibition of HDAC6 and in the treatment of various diseases, disorders or conditions related to HDAC6.

8 Claims, No Drawings