US009409921B2

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

(10) **Patent No.: US 9,409,921 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **2,4-DISUBSTITUTED PYRIMIDINES AS KINASE INHIBITORS**

(71) Applicant: **Celgene Avilomics Research, Inc.**, Bedford, MA (US)

(72) Inventors: **Juswinder Singh**, Ashland, MA (US); **Russell Petter**, Stow, MA (US); **Richland Wayne Tester**, Marlborough, MA (US); **Arthur F. Kluge**, Lincoln, MA (US); **Hormoz Mazdiyasni**, Marlborough, MA (US); **William Frederick Westlin, III**, Boxborough, MA (US); **Deqiang Niu**, Lexington, MA (US); **Lixin Qiao**, Tewksbury, MA (US)

(73) Assignee: **Celgene Avilomics Research, Inc.**, 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 146 days.

(21) Appl. No.: **14/253,903**

(22) Filed: **Apr. 16, 2014**

(65) **Prior Publication Data**

US 2014/0213574 A1 Jul. 31, 2014

Related U.S. Application Data

(60) Continuation of application No. 13/667,396, filed on Nov. 2, 2012, now Pat. No. 8,710,222, which is a division of application No. 12/648,693, filed on Dec. 29, 2009, now Pat. No. 8,338,439, which is a continuation-in-part of application No. 12/492,180, filed on Jun. 26, 2009, now Pat. No. 8,450,335.

(60) Provisional application No. 61/170,874, filed on Apr. 20, 2009, provisional application No. 61/148,388, filed on Jan. 29, 2009, provisional application No. 61/076,450, filed on Jun. 27, 2008.

(51) **Int. Cl.**

A61K 31/505	(2006.01)
C07D 495/04	(2006.01)
C07D 239/47	(2006.01)
C07D 239/48	(2006.01)
C07D 401/14	(2006.01)
C07D 403/12	(2006.01)
C07D 407/12	(2006.01)
C07D 413/12	(2006.01)
C07D 413/14	(2006.01)
C07D 471/04	(2006.01)
C07D 487/04	(2006.01)
C07D 487/18	(2006.01)
A61K 31/506	(2006.01)
A61K 31/519	(2006.01)
A61K 31/5377	(2006.01)
A61K 31/538	(2006.01)
A61K 31/541	(2006.01)
A61K 45/06	(2006.01)
C07D 401/12	(2006.01)
C07D 405/12	(2006.01)
C07D 405/14	(2006.01)
C07D 487/08	(2006.01)

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

CPC ***C07D 495/04*** (2013.01); ***A61K 31/505*** (2013.01); ***A61K 31/506*** (2013.01); ***A61K 31/519*** (2013.01); ***A61K 31/538*** (2013.01); ***A61K 31/5377*** (2013.01); ***A61K 31/541*** (2013.01); ***A61K 45/06*** (2013.01); ***C07D 239/47*** (2013.01); ***C07D 239/48*** (2013.01); ***C07D 401/12*** (2013.01); ***C07D 401/14*** (2013.01); ***C07D 403/12*** (2013.01); ***C07D 405/12*** (2013.01); ***C07D 405/14*** (2013.01); ***C07D 407/12*** (2013.01); ***C07D 413/12*** (2013.01); ***C07D 413/14*** (2013.01); ***C07D 471/04*** (2013.01); ***C07D 487/04*** (2013.01); ***C07D 487/08*** (2013.01); ***C07D 487/18*** (2013.01)

(58) **Field of Classification Search**

CPC A61K 31/505

USPC 514/235.8, 252.14, 275, 326, 397, 461

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,879,303	A	11/1989	Davison et al.
5,958,935	A	9/1999	Davis et al.
6,093,716	A	7/2000	Davis et al.
6,114,333	A	9/2000	Davis et al.
6,127,376	A	10/2000	Davey et al.
6,160,010	A	12/2000	Uckun et al.
6,262,088	B1	7/2001	Phillips
6,469,168	B1	10/2002	Ratzne Simonek et al.
6,579,983	B1	6/2003	Batchelor et al.
6,593,326	B1	7/2003	Bradbury et al.

(Continued)

FOREIGN PATENT DOCUMENTS

AU	2009251863	A1	12/2009
CN	102558149	A	7/2012

(Continued)

OTHER PUBLICATIONS

Jordan, V. C. Nature Reviews: Drug Discovery, 2, 2003, 205.*

(Continued)

Primary Examiner — Douglas M Willis

(74) *Attorney, Agent, or Firm* — Choate, Hall & Stewart LLP; Kristen C. Buteau

(57) **ABSTRACT**

The present invention provides 2,4-disubstituted pyrimidine compounds useful as kinase inhibitors, pharmaceutically acceptable compositions thereof, and methods of using the same.

2 Claims, 29 Drawing Sheets