US009409887B2

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

(10) **Patent No.: US 9,409,887 B2**
(45) **Date of Patent: *Aug. 9, 2016**

(54) **MUTANT-SELECTIVE EGFR INHIBITORS AND USES THEREOF**

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

(72) Inventors: **Kwangho Lee**, Daejeon (KR); **Deqiang Niu**, Lexington, MA (US); **Matthew F. Baevsky**, Northborough, 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 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/448,578**

(22) Filed: **Jul. 31, 2014**

(65) **Prior Publication Data**

US 2015/0025055 A1 Jan. 22, 2015

Related U.S. Application Data

(63) Continuation of application No. 13/291,706, filed on Nov. 8, 2011, now Pat. No. 8,796,255.

(60) Provisional application No. 61/534,330, filed on Sep. 13, 2011, provisional application No. 61/412,388, filed on Nov. 10, 2010.

(51) **Int. Cl.**

C07D 403/12	(2006.01)
C07D 239/48	(2006.01)
C12N 9/12	(2006.01)
A61K 31/155	(2006.01)
A61K 45/06	(2006.01)
C07D 239/42	(2006.01)
C07D 239/47	(2006.01)

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

CPC ***C07D 403/12*** (2013.01); ***A61K 31/155*** (2013.01); ***A61K 45/06*** (2013.01); ***C07D 239/42*** (2013.01); ***C07D 239/47*** (2013.01); ***C07D 239/48*** (2013.01); ***C12N 9/12*** (2013.01); *C12Y 207/10* (2013.01)

(58) **Field of Classification Search**

CPC .. C07D 403/12; C07D 239/48; C07D 239/47; C12N 9/12

USPC 514/210.2, 272, 275; 435/184

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.
6,838,464	B2	1/2005	Pease et al.
6,939,874	B2	9/2005	Harmange et al.
7,060,827	B2	6/2006	Singh et al.
7,122,542	B2	10/2006	Singh et al.
7,125,879	B2	10/2006	Guillemont et al.
7,176,212	B2	2/2007	Breault et al.
7,202,033	B2	4/2007	Prescott et al.
7,241,769	B2	7/2007	Stadtmueller et al.
7,282,504	B2	10/2007	Armistead et al.
7,329,671	B2	2/2008	Singh et al.
7,329,672	B2	2/2008	Singh et al.
7,332,484	B2	2/2008	Singh et al.
7,435,814	B2	10/2008	Singh et al.
7,452,879	B2	11/2008	Singh et al.
7,485,724	B2	2/2009	Singh et al.
7,491,732	B2	2/2009	Li et al.
7,498,435	B2	3/2009	Singh et al.
7,504,396	B2	3/2009	Nunes et al.
7,514,444	B2	4/2009	Honigberg et al.
7,514,445	B2	4/2009	Freyne et al.
7,514,446	B2	4/2009	Davis-Ward et al.
7,517,886	B2	4/2009	Singh et al.
7,528,143	B2	5/2009	Noronha et al.
7,531,548	B2	5/2009	Guillemont et al.
7,550,460	B2	6/2009	Singh et al.
7,557,210	B2	7/2009	Singh et al.
7,582,648	B2	9/2009	Singh et al.
7,589,200	B2	9/2009	Singh et al.
7,642,351	B2	1/2010	Singh et al.

(Continued)

FOREIGN PATENT DOCUMENTS

CN	102558149	7/2012
CN	103159742	6/2013

(Continued)

OTHER PUBLICATIONS

Hackam, et al. JAMA, 296(14), 2006, 1731-1732.*

Jordan, V. C. Nature Reviews: Drug Discovery, 2, 2003, 205-213.*

U.S. Appl. No. 13/518,833, filed Jun. 22, 2012, Gray et al.

U.S. Appl. No. 14/253,903, filed Apr. 16, 2014, Singh et al.

Aliagas-Martin, I. et al., A class of 2,4-bisanilinopyrimidine Aurora A inhibitors with unusually high selectivity against Aurora B, J. Med. Chem. 52:3300-3307 (2009).

Andrulis, I. et al., Neu/ErbB-2 amplification identifies a poor-prognosis group of women with node-negative breast cancer, J Clin Oncol 16:1340-9 (1998).

Bamborough, P. et al., N-4-Pyrimidinyl-1H-indazol-4-amine inhibitors of Lck: Indazoles as phenol isosteres with improved pharmacokinetics, Bioorg. & Med. Chem. Lett. 17:4363-4368 (2007).

(Continued)

Primary Examiner — James O Wilson

Assistant Examiner — Ebenezer O Sackey

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

(57) **ABSTRACT**

The present invention provides compounds, pharmaceutically acceptable compositions thereof, and methods of using the same.

26 Claims, No Drawings