US009409924B2

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

(10) **Patent No.: US 9,409,924 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **SELECTIVE GLYCOSIDASE INHIBITORS AND USES THEREOF**

(75) Inventors: **Tong-Shuang Li**, Burnaby (CA); **Ernest McEachern**, Burnaby (CA); **David Vocadlo**, Burnaby (CA); **Yuanxi Zhou**, Burnaby (CA); **Yongbao Zhu**, Burnaby (CA); **Harold Selnick**, West Point, PA (US)

(73) Assignees: **Alectos Therapeutics Inc.**, Burnaby (CA); **Merck Sharp & Dohme Corp.**, Rahway, NJ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 21 days.

(21) Appl. No.: **14/129,177**

(22) PCT Filed: **Jun. 27, 2012**

(86) PCT No.: **PCT/CA2012/050433**

§ 371 (c)(1),
(2), (4) Date: **May 19, 2014**

(87) PCT Pub. No.: **WO2013/000084**

PCT Pub. Date: **Jan. 3, 2013**

(65) **Prior Publication Data**

US 2014/0296205 A1 Oct. 2, 2014

Related U.S. Application Data

(60) Provisional application No. 61/501,377, filed on Jun. 27, 2011.

(51) **Int. Cl.**

C07D 513/04	(2006.01)
C07H 9/06	(2006.01)
C07H 13/04	(2006.01)
C07H 13/12	(2006.01)
C07H 15/18	(2006.01)
C12Q 1/34	(2006.01)
C12Q 1/48	(2006.01)
C12Q 1/37	(2006.01)
G01N 33/50	(2006.01)

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

CPC ***C07D 513/04*** (2013.01); ***C07H 9/06*** (2013.01); ***C12Q 1/34*** (2013.01); ***C12Q 1/37*** (2013.01); ***G01N 33/5038*** (2013.01); *G01N 2333/924* (2013.01); *G01N 2500/04* (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

8,334,310	B2	12/2012	Vocadlo et al.	
8,541,441	B2	9/2013	Vocadlo et al.	
8,927,507	B2 *	1/2015	McEachern et al.	514/23
8,933,040	B2	1/2015	Coburn et al.	
8,962,664	B2	2/2015	Vocadlo et al.	
2008/0287375	A1	11/2008	Vocadlo et al.	
2010/0016386	A1	1/2010	Vocadlo et al.	
2011/0237631	A1	9/2011	Vocadlo et al.	
2011/0301217	A1	12/2011	Vocadlo et al.	
2012/0316207	A1	12/2012	Vocadlo et al.	
2013/0131044	A1	5/2013	Li et al.	
2014/0005191	A1	1/2014	Coburn et al.	
2014/0018309	A1	1/2014	Kaul et al.	
2014/0051719	A1	2/2014	Vocadlo et al.	
2014/0088028	A1	3/2014	Kaul et al.	
2014/0107044	A1	4/2014	McEachern et al.	
2014/0206665	A1	7/2014	Selnick et al.	
2014/0275022	A1	9/2014	Li et al.	
2014/0296205	A1	10/2014	Li et al.	
2015/0045346	A1	2/2015	Li et al.	

FOREIGN PATENT DOCUMENTS

CA	2599843	A1	9/2006
CA	2661582	A1	3/2008
CN	101208352	A	6/2008
CN	101595111	A	12/2009
CN	103339138	A	10/2013
JP	01-180894	A	7/1989
JP	07-316178	A	12/1995
JP	09-132585	A	5/1997
JP	2002-338532	A	11/2002
JP	2003-12683	A	1/2003
WO	WO-2006/016904	A2	2/2006
WO	WO-2006/092049	A1	9/2006
WO	WO-2008/025170	A1	3/2008
WO	WO-2010/012106	A1	2/2010
WO	WO-2010/012107	A1	2/2010
WO	WO-2010/037207	A1	4/2010
WO	WO-2011/140640	A1	11/2011
WO	WO-2012/061927	A1	5/2012
WO	WO-2012/061971	A1	5/2012
WO	WO-2012/061972	A1	5/2012

(Continued)

OTHER PUBLICATIONS

International Search Report for International Application No. PCT/CA2012/000267, mailed Apr. 5, 2012 (7 pages).

Written Opinion of the International Searching Authority for International Application No. PCT/CA2012/000267, mailed Jul. 11, 2012 (7 pages).

Communication pursuant to Article 94(3) EPC for European Application No. 07800577.4, dated Aug. 17, 2010 (16 pages).

Summons to attend oral proceedings pursuant to Rule 115(1) EPC for European Application No. 07800577.4, dated May 3, 2011 (10 pages).

Office Action for Canadian Application No. 2,661,582, dated Sep. 9, 2013 (5 pages).

(Continued)

Primary Examiner — Traviss C McIntosh, III

(74) *Attorney, Agent, or Firm* — Clark & Elbing LLP

(57) **ABSTRACT**

The invention provides compounds with enhanced permeability for selectively inhibiting glycosidases, prodrugs of the compounds, and pharmaceutical compositions including the compounds or prodrugs of the compounds. The invention also provides methods of treating diseases and disorders related to deficiency or overexpression of O-GlcNAcase, accumulation or deficiency of O-GlcNAc.

21 Claims, No Drawings