US009284305B2

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

(10) **Patent No.: US 9,284,305 B2**
(45) **Date of Patent: *Mar. 15, 2016**

(54) **METHODS OF TREATING OCULAR DISEASES USING DERIVATIVES OF LIPOIC ACID**

(71) Applicant: **Encore Health, LLC**, Roanoke, VA (US)

(72) Inventors: **William Garner**, Eastport, ME (US); **Margaret Garner**, Eastport, ME (US); **George Minno**, Windham, NH (US); **David Gooden**, Durham, NC (US)

(73) Assignee: **Encore Health, LLC**, Roanoke, VA (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.: **14/303,405**

(22) Filed: **Jun. 12, 2014**

(65) **Prior Publication Data**

US 2014/0357691 A1 Dec. 4, 2014
US 2015/0246903 A9 Sep. 3, 2015

Related U.S. Application Data

(62) Division of application No. 12/815,586, filed on Jun. 15, 2010, now Pat. No. 8,795,706.

(60) Provisional application No. 61/187,005, filed on Jun. 15, 2009, provisional application No. 61/187,018, filed on Jun. 15, 2009, provisional application No. 61/187,023, filed on Jun. 15, 2009, provisional application No. 61/186,986, filed on Jun. 15, 2009, provisional application No. 61/187,028, filed on Jun. 15, 2009, provisional application No. 61/187,033, filed on Jun. 15, 2009, provisional application No. 61/187,039, filed on Jun. 15, 2009, provisional application No. 61/186,940, filed on Jun. 15, 2009, provisional application No. 61/224,930, filed on Jul. 13, 2009, provisional application No. 61/235,051, filed on Aug. 19, 2009, provisional application No. 61/237,912, filed on Aug. 28, 2009, provisional application No. 61/242,232, filed on Sep. 14, 2009.

(51) **Int. Cl.**

A61F 2/02	(2006.01)
C07D 409/12	(2006.01)
A61K 31/765	(2006.01)
A61K 9/00	(2006.01)
A61K 31/095	(2006.01)
A61K 31/381	(2006.01)
A61K 31/382	(2006.01)
A61K 31/385	(2006.01)
A61K 31/4178	(2006.01)
A61K 31/497	(2006.01)
A61K 31/5377	(2006.01)
A61K 31/67	(2006.01)
A61K 31/70	(2006.01)
A61K 31/4025	(2006.01)
A61K 45/06	(2006.01)
C07D 339/04	(2006.01)
A61N 5/06	(2006.01)
A61N 5/067	(2006.01)

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

CPC ***C07D 409/12*** (2013.01); ***A61K 9/0048*** (2013.01); ***A61K 31/095*** (2013.01); ***A61K 31/381*** (2013.01); ***A61K 31/382*** (2013.01); ***A61K 31/385*** (2013.01); ***A61K 31/4025*** (2013.01); ***A61K 31/4178*** (2013.01); ***A61K 31/497*** (2013.01); ***A61K 31/5377*** (2013.01); ***A61K 31/67*** (2013.01); ***A61K 31/70*** (2013.01); ***A61K 31/765*** (2013.01); ***A61K 45/06*** (2013.01); ***C07D 339/04*** (2013.01); *A61N 5/0613* (2013.01); *A61N 2005/067* (2013.01)

(58) **Field of Classification Search**

CPC A61K 9/0048; A61K 31/765
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,238,224	A	3/1966	Ohara et al.
3,855,240	A	12/1974	Mueller
4,210,667	A	7/1980	Sarges et al.
4,755,528	A	7/1988	DuPriest et al.
5,395,356	A	3/1995	King et al.
5,459,133	A	10/1995	Neufeld
5,465,737	A	11/1995	Schachar

(Continued)

FOREIGN PATENT DOCUMENTS

EP	0 369 880	5/1990
WO	WO 93/25166	12/1993

(Continued)

OTHER PUBLICATIONS

Al-Ghoul, K. J., R. K. Nordgren, A. J. Kuszak, C. D. Freel, M. J. Costello, and J. R. Kuszak. 2001. Structural evidence of human nuclear fiber compaction as a function of ageing and cataractogenesis. Experimental eye research 72: 199-214.

Applegate, M. A., K. M. Humphries, and L. I. Szweda. Jan. 2007. Reversible Inhibition of alpha-Ketoglutarate Dehydrogenase by Hydrogen Peroxide: Glutathionylation and Protection of Lipoic Acid. Biochemistry. 47(1): 473-478.

Argirova, M., M. Kleine-Reidick, and W. Breipohl. 2004. Redox status of the eye lens: a regional study. Cell biochemistry and biophysics 41: 381-390.

(Continued)

Primary Examiner — Carlos Azpuru

(74) *Attorney, Agent, or Firm* — Sterne, Kessler, Goldstein & Fox P.L.L.C.

(57) **ABSTRACT**

Dithiol compounds and derivatives thereof are disclosed. The agents are useful for treating an ocular disease, especially presbyopia and cataract. Also provided are methods of treating an ocular disease, the methods comprising administering to a subject an active agent and an adjunctive agent.

35 Claims, 5 Drawing Sheets