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(12) **United States Patent**
Laine et al.(10) **Patent No.:** **US 8,183,257 B2**
(45) **Date of Patent:** **May 22, 2012**(54) **MUSCARINIC ACETYLCHOLINE
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Middlesex (GB)(*) Notice: Subject to any disclaimer, the term of this
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27, 2004.(51) **Int. Cl.**
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See application file for complete search history.

(56) **References Cited****U.S. PATENT DOCUMENTS**

2,800,478 A 7/1957 Zirkle et al.
2,800,481 A 7/1957 Zirkle et al.
3,634,852 A 1/1972 Hartley et al.
5,590,645 A 1/1997 Davies et al.
5,780,466 A 7/1998 Emonds-Alt et al.
5,860,419 A 1/1999 Davies et al.
5,873,360 A 2/1999 Davies et al.
6,248,752 B1 6/2001 Smith
6,262,066 B1 7/2001 Tulshian et al.
6,350,758 B1 2/2002 Kozikowski et al.
6,455,527 B2 9/2002 Tulshian et al.
6,696,462 B2 2/2004 Eickmeier et al.
6,750,226 B2 6/2004 Forner et al.
6,951,868 B2 10/2005 Walker et al.
7,232,841 B2 6/2007 Busch-Petersen et al.
7,276,521 B2 10/2007 Busch-Petersen et al.
7,439,255 B2 10/2008 Wan et al.
2005/0020660 A1 1/2005 Guyaux et al.
2005/0113417 A1 5/2005 Mammen et al.
2005/0209272 A1 9/2005 Fernandez et al.
2005/0277676 A1 12/2005 Laine et al.
2006/0160844 A1 7/2006 Belmonte et al.
2006/0178395 A1 8/2006 Belmonte et al.
2006/0178396 A1 8/2006 Belmonte et al.

2007/0135478 A1 6/2007 Palovich et al.
2007/0149598 A1 6/2007 Busch-Petersen et al.
2007/0173646 A1 7/2007 Laine et al.
2007/0179131 A1 8/2007 Jin et al.
2007/0179180 A1 8/2007 Busch-Petersen et al.
2007/0179184 A1 8/2007 Busch-Petersen et al.
2007/0185088 A1 8/2007 Busch-Petersen et al.
2007/0185090 A1 8/2007 Busch-Petersen et al.
2007/0185148 A1 8/2007 Busch-Petersen et al.
2007/0185155 A1 8/2007 Laine et al.
2007/0232599 A1 10/2007 Palovich et al.
2007/0238751 A1 10/2007 Laine et al.
2007/0238752 A1 10/2007 Busch-Petersen et al.
2007/0244150 A1 10/2007 Busch-Petersen et al.
2007/0249664 A1 10/2007 Laine et al.
2007/0270456 A1 11/2007 Wan et al.
2007/0293531 A1 12/2007 Busch-Petersen et al.
2008/0194618 A1 8/2008 Laine et al.
2008/0234315 A1 9/2008 Busch-Petersen et al.
2008/0249127 A1 10/2008 Laine et al.
2008/0275079 A1 11/2008 Busch-Petersen et al.
2008/0287487 A1 11/2008 Cooper et al.

FOREIGN PATENT DOCUMENTS

EP 0069715 6/1982
GB 2064336 6/1981
GB 2129691 5/1984
GB 2169265 7/1986
GB 2178965 2/1987
GB 2242134 9/1991
WO 87/05213 9/1987
WO 01/04118 1/2001
WO 02/53564 7/2002
WO 03/087094 10/2003
WO 2005/087236 3/2005
WO 2006/050239 5/2006
WO 2006/055503 5/2006
WO 2006/055553 5/2006
WO 2006/062883 6/2006
WO 2006/062931 6/2006
WO 2006/065755 6/2006
WO 2006/065788 6/2006

(Continued)

OTHER PUBLICATIONS

Ronald B. George "Chest Medicine: Essentials of Pulmonary and
Critical Care Medicine", 5th Ed., May 2005, p. 173.*
Langmead CJ, Watson J, Reavill C. Muscarinic acetylcholine recep-
tors as CNS drug targets. *Pharmacol. Ther.* Feb 2008, 117 (2) 232-
43.*
Brown, *History and Basic Properties*, Humana Press, USA pp. 7-9
(1989).
Caulfield, *Pharmac. Ther.*, vol. 58 pp. 319-379 (1993).
Costello, et al., *American Journal of Physiology*, vol. 276 (5) pp.
L709-L714 (1999).
Fryer and Jacoby, *Am J Respir Crit Care Med*, vol. 158 (5, pt 3) pp.
154-160 (1998).
Fryer et al., *Life Sci*, vol. 64 (6-7) pp. 449-455 (1999).
Hedge, et al., *Life Sciences*, vol. 64 (6/7) pp. 419-428 (1999).
Ikeda, et al., *Naunyn-Schmiedeberg's Arch Pharmacol.*, vol. 366, pp.
97-103, (2002).

(Continued)

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Furman(57) **ABSTRACT**Muscarinic Acetylcholine Receptor Antagonists and methods
of using them are provided.**31 Claims, No Drawings**