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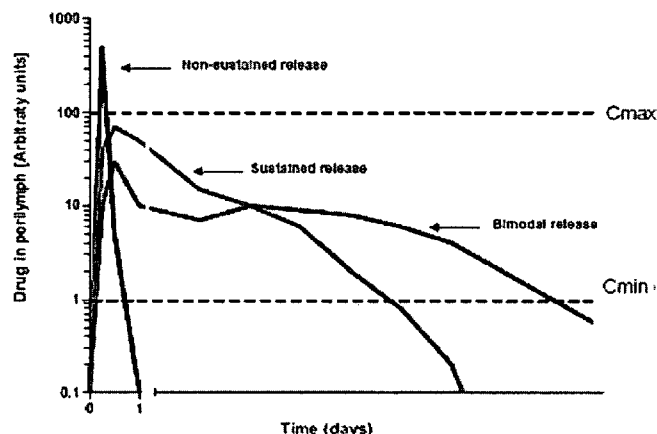
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[Continued on next page]

(54) Title: CONTROLLED-RELEASE APOPTOSIS MODULATING COMPOSITIONS AND METHODS FOR THE TREATMENT OF OTIC DISORDERS

FIGURE 1



(57) Abstract: Disclosed herein are compositions and methods for the treatment of otic disorders with apoptosis modulating agent compositions and compositions administered locally to an individual afflicted with an otic disorder, through direct application of these compositions and compositions onto or via perfusion into the targeted auris structure(s).



TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

(88) Date of publication of the international search report:

1 April 2010

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/050077**A. CLASSIFICATION OF SUBJECT MATTER****A61K 9/16(2006.01)i, A61P 27/16(2006.01)i, A61K 38/22(2006.01)i, A61K 38/48(2006.01)i**

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC above

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKIPASS, Pubmed

* Key words: otic, ear, apoptosis, polyoxyethylene, polyoxypropylene, copolymer, gel, formulation

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2004/0101560 A1 (RONALD J. SAWCHUK AND BELINDA W.Y.CHEUNG) 27 May 2004 See the abstract, [0016]-[0019] in description, examples 1-3, and claims 1-11.	1 - 13
Y	US 5,292,516 A (MEDIVENTURES, INC.) 08 March 1994 See the abstract, columns 5 and 6, examples 1-5, and claims.	1 - 13
Y	US 2003/0229333 A1 (CONTROL DELIVERY SYSTEMS, INC) 11 December 2003 See the abstract, [0030], [0111], [0126], and claims 1, 14, 18 and 31.	1 - 13
Y	US 2005/0095270 A1 (HINRICH STAECKER) 05 May 2005 See the abstract, [0037], [0040], claims 1, 3, 6-8.	1 - 13
A	US 2004/0106542 A1 (THE PENN STATE RESEARCH FOUNDATION) 03 June 2004 See the whole document.	1 - 13
E	US 2009/0246255 A1 (THOMAS MEYER) 01 October 2009 See the whole document.	1 - 13



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

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"E" earlier application or patent but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2009/050077**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 14-19
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 14-19 are directed to a method of treating an otic disease by administering the anti-apoptotic agent to the patients, and thus relate to a subject matter which this International Searching Authority is not required to search under Article 17(2)(a)(i) of the PCT and Rule 39.1(v) of the Regulations under the PCT.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2009/050077

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004-0101560 A1	27.05.2004	AU 2003-298712 A1	23.06.2004
		AU 2003-298712 A8	23.06.2004
		CA 2505298 A1	17.06.2004
		EP 1569618 A2	07.09.2005
		JP 2006-509791 T	23.03.2006
		JP 2006-509791 A	23.03.2006
		US 07220431 B2	22.05.2007
		US 2007-0098679 A1	03.05.2007
		WO 2004-050021 A3	29.07.2004
		WO 2004-050021 A2	17.06.2004
		WO 2004-050021 A3	17.06.2004
US 05292516 A	08.03.1994	EP 0455396 B1	29.01.1997
		EP 0455396 A1	06.11.1991
		JP 04-225914 A	14.08.1992
		JP 02-753152 B2	27.02.1998
		JP 2753152 B2	18.05.1998
		US 05306501 A	26.04.1994
		US 05300295 A	05.04.1994
		US 05298260 A	29.03.1994
		US 05593683 A	14.01.1997
US 2003-0229333 A1	11.12.2003	US 2007-0160648 A1	12.07.2007
US 2005-095270 A1	05.05.2005	US 07387614 B2	17.06.2008
US 2004-0106542 A1	03.06.2004	US 2005-0232872 A1	20.10.2005
		US 06387390 B1	14.05.2002
		US 06652873 B2	25.11.2003
		US 06908623 B2	21.06.2005
		US 2002-0114803 A1	22.08.2002
Us 2009-0246255 A1	01.10.2009	NONE	