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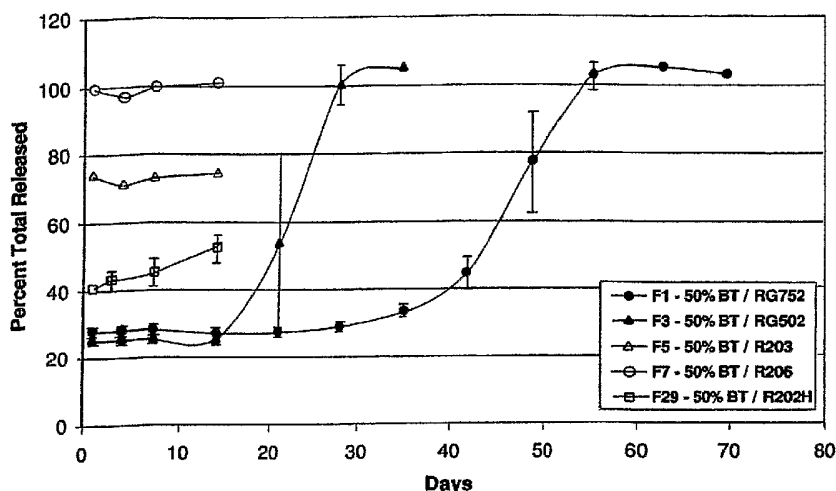
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[Continued on next page]

(54) Title: SUSTAINED RELEASE INTRAOCULAR IMPLANTS AND METHODS FOR PREVENTING RETINAL DYSFUNCTION



(57) Abstract: Biocompatible intraocular microspheres and implants include an alpha-2 adrenergic receptor agonist and a polymer associated with the alpha-2 adrenergic receptor agonist to facilitate release of the alpha-2 adrenergic receptor agonist into an eye for an extended period of time. The alpha-2 adrenergic receptor agonist may be associated with a biodegradable polymer matrix, such as a matrix of two biodegradable polymers. The implants may be placed in an eye to treat or to prevent the occurrence of one or more ocular conditions, to reduce one or more symptoms of an ocular condition, such as an ocular neurosensory disorder and the like, to enhance normal retinal function and/or to lower intraocular pressure.

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INTERNATIONAL SEARCH REPORT

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

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2004/066979 A (CONTROL DELIVERY SYSTEMS, INC; ASHTON, PAUL; GUO, HONG) 12 August 2004 (2004-08-12) page 15, line 21 - line 24 page 16, line 10 - line 25 page 22, line 21; claims -----	1-58
X	WO 03/077952 A (NOVARTIS AG; NOVARTIS PHARMA GMBH; KIS, GYÖRGY LAJOS; SCHÖCH, CHRISTI) 25 September 2003 (2003-09-25) page 6, paragraphs 1,4 page 7, last paragraph -----	1-58
Y	EP 0 992 244 A (SANTEN PHARMACEUTICAL CO., LTD) 12 April 2000 (2000-04-12) paragraph [0005] - paragraph [0014]; figures -----	1-58
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MERKLI A ET AL: "USE OF INSOLUBLE BIODEGRADABLE POLYMERS IN OPHTHALMIC SYSTEMS FOR THE SUSTAINED RELEASE OF DRUGS" EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL, vol. 41, no. 5, 1 October 1995 (1995-10-01), pages 271-283, XP000535194 ISSN: 0939-6411 the whole document -----	1-58
Y	WO 02/36162 A (ALLERGAN SALES, INC; ALLERGAN, INC) 10 May 2002 (2002-05-10) the whole document -----	1-58
Y	US 2002/111357 A1 (WHEELER LARRY A ET AL) 15 August 2002 (2002-08-15) the whole document -----	1-58

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2005/014605

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2004066979	A	12-08-2004	AU 2004207506 A1 BR 0406879 A CA 2513751 A1 EP 1592408 A2	12-08-2004 03-01-2006 12-08-2004 09-11-2005
WO 03077952	A	25-09-2003	AU 2003214133 A1 BR 0308486 A CA 2479351 A1 CN 1642578 A JP 2005523299 T	29-09-2003 18-01-2005 25-09-2003 20-07-2005 04-08-2005
EP 0992244	A	12-04-2000	CA 2294714 A1 WO 9901156 A1 NO 996569 A US 6488938 B1	14-01-1999 14-01-1999 28-02-2000 03-12-2002
WO 0236162	A	10-05-2002	AU 3056702 A CA 2427655 A1 EP 1353692 A2 JP 2004512378 T WO 02058730 A2	15-05-2002 10-05-2002 22-10-2003 22-04-2004 01-08-2002
US 2002111357	A1	15-08-2002	NONE	