

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
21 February 2008 (21.02.2008)

PCT

(10) International Publication Number  
**WO 2008/022256 A3**

(51) **International Patent Classification:**  
**A61K 31/436** (2006.01)

(21) **International Application Number:**

**PCT/US2007/076094**

(22) **International Filing Date:** 16 August 2007 (16.08.2007)

(25) **Filing Language:** English

(26) **Publication Language:** English

(30) **Priority Data:**

60/837,859 16 August 2006 (16.08.2006) US  
60/878,638 5 January 2007 (05.01.2007) US

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(81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, **BR**, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, **HR**, HU, **ID**, IL, IN, IS, **JP**, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

(84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— *with international search report*

(88) **Date of publication of the international search report:**  
14 August 2008

(54) **Title:** METHODS AND COMPOSITIONS FOR PREVENTING OR TREATING AGE-RELATED DISEASES

(57) **Abstract:** The invention provides methods for treating or preventing an age-related disease, condition, or disorder comprising administering a therapeutically effective amount of an inhibitor of TOR to a patient in need thereof. The invention also provides pharmaceutical compositions and topical formulations for treating or preventing an age-related disease, condition, or disorder comprising an inhibitor of TOR and a pharmaceutically acceptable carrier. In particular, the invention provides methods, pharmaceutical compositions, and topical formulations comprising rapamycin or an analog of rapamycin.

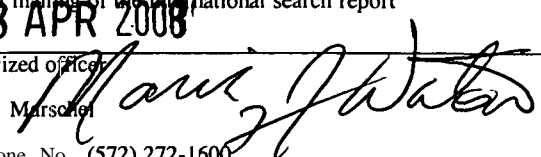


**WO 2008/022256 A3**

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/76094

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC: <b>A61K 31/436</b> (2006.01)  USPC: 514/291 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. :  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) Please See Continuation Sheet		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
<b>X</b>	US 7,026,374 B2 (Nathan et al.) 11 Apr 2006 (11.04.2006, abstract; col. 6, line 25, 37-39, 64-66; col. 7, lines 12-13, 21-23; col. 8, line 1; claims 1, 10, 18	1-7, 9-15, 17-21
<b>X</b>	US 7,074,804 B2 (Zhu et al.) 11 Jul 2006 (11.07.2006), col 2, lines 1-50; col. 5, line 52; col. 6, lines 46-48, 65; col. 7, line 48; col. 8, line 39; col. 10, lines 9-23, 65	1-22
<input type="checkbox"/> Further documents are listed in the continuation of Box-C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"E"	earlier application or patent published on or after the international filing date	"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
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"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
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 20 March 2008 (20.03.2008)		Date of mailing of the international search report <b>08 APR 2008</b>
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer Ardin Marscher  Telephone No. (572) 272-1600

**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.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
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:  
Please See Continuation Sheet

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 additional fees, this Authority did not invite payment of any additional fees.
  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.

**BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-8, 17-22, drawn to a topical formulation/pharmaceutical composition.

Group II, claim(s) 9-16, drawn to a method for treating or preventing an age-related disease condition or disorder.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

If Group II is elected also elect:

(i) a single age-related disease or condition from species recited in claims 5-6, and 12.

The claims are deemed to correspond to the species listed above in the following manner:

Conditions as recited in claims 5-6, 12-14 and 20

The following claim(s) are generic: all claims are generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The technical feature linking Groups I-II is a formulation comprising a TOR inhibitor. Nathan et al. (US 7,026,374 B2; 2006 Apr 11) teaches pharmaceutical compositions that contain rapamycin as the bioactive agent (abstract; claim 18). Rapamycin inherently is a TOR inhibitor, as disclosed and claimed by applicant. Therefore, since the prior art teaches the technical feature the technical feature lacks novelty and does not constitute a "special" technical feature.

Accordingly Groups I-II are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The technical feature linking the species is an age-related disease that can be treated by a TOR inhibitor. Zhu et al. (US 7,074,804 B2; 2006 Jul 11) teaches pharmaceutical compositions containing CCI-779 Isomer C (a rapamycin derivative; abstract); the compositions are useful for the treatment of various conditions and diseases, including psoriasis (col. 5, line 52). Therefore, the technical feature linking the species does not constitute a special technical feahire as is does not define a contribution over the prior art.

Accordingly, the species are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

Continuation of B. FIELDS SEARCHED Item 3:

WEST

search terms: rapamycin, everolimus, tacrolimus, cci-779, abt-578, ap-23573, keratosis, keloid, psoriasis, karposi's sarcoma, age related spots, pigment spots, wrinkles, photo-aged skin, angiogenic spots, vitamin e, vitamin a, antibacterial antibiotic, antioxidant, l-carnitine, lipoic acid, metformine, resveratrol, leptine, NSAID, cox inhibitor, topical, pharmaceutical composition, carrier, water