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(71) Applicant: **UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INC.** [US/US]; 223 Grinter Hall, Gainesville, FL 32611 (US).

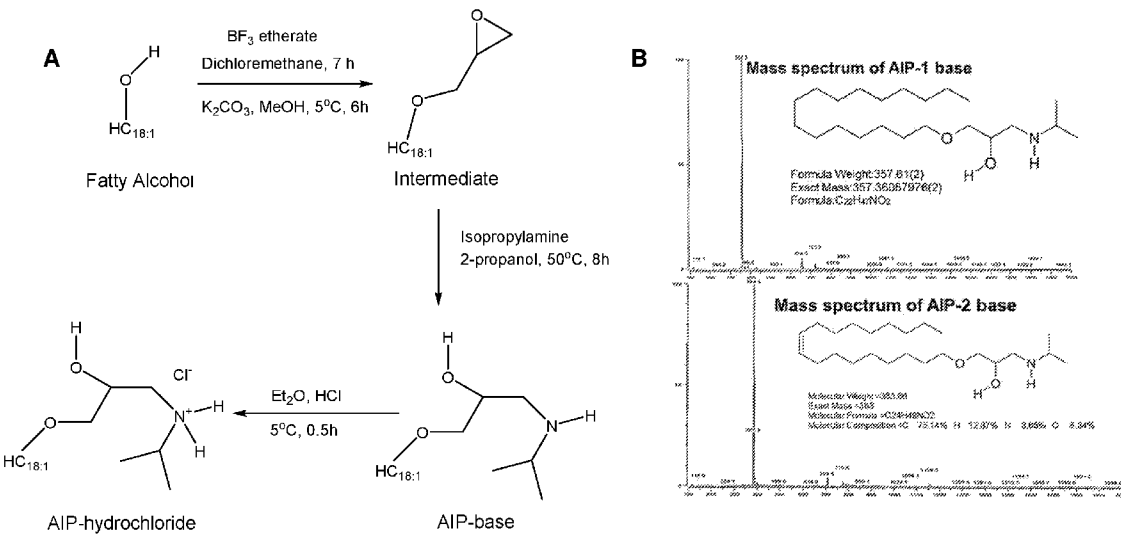
(72) Inventor: **SVETLOV, Stanislav Igorevich**; 9710 SW 55th Road, Gainesville, FL 32608 (US).

(74) Agent: **VAN DYKE, Timothy H.** et al.; Beusse, Wolter, Sanks & Maire, P.A., 390 N. Orange Ave., Suite 2500, Orlando, FL 32801 (US).

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(54) Title: COMPOSITIONS AND METHODS FOR TREATMENT OF CENTRAL NERVOUS SYSTEM TUMORS

FIG. 3



(57) **Abstract:** Compounds, pharmaceutical compositions, and methods for treating cancer, in particular brain cancer, are provided, including amphiphilic fatty acid/alcohol ethers (AIPs) comprising endocannabinoid and FABP motifs covalently linked to a beta-adrenoreceptor antagonist motif in one molecule. The invention includes methods for inhibiting growth of brain cancer cells by contacting the compound(s) with brain cancer cells. The invention provides a method for treating both brain cancer and brain cancer metastases, and for suppression of regrowth of brain cancer cells after radiation, surgical treatment, or chemotherapy of brain cancer. The invention also comprises an optimized chemical synthesis of the AIP compounds and methods of using the compounds, alone or in combination with another agent, for suppressing the growth of brain cancer cells, and enhancing survival of normal CNS cells, or improving recuperation from radiation, surgical or chemotherapy.

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[Continued on next page]

OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Published:

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

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/043120

A. CLASSIFICATION OF SUBJECT MATTER

A61K 31/131(2006.01)i, C07C 217/28(2006.01)i, C07C 217/46(2006.01)i, A61P 35/00(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)
A61K 31/131; A61K 31/13; A61K 31/133; A61K 31/202; A61P 3/10; C07C 217/28; C07C 93/04; C07C 217/46; A61P 35/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords:fatty acid, lipid, isopropyl, brain cancer, tumor, tosylate, glycidyl

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011-0177108 A1 (SVETLOV, S. I. et al.) 21 July 2011 See claims 40-59; paragraphs [0003], [0033], [0052], [0277], [0278], [0282], [0286]; and figures 1, 6A.	1-6
Y		7
Y	BYUN, H.-S. et al., "A Two-step synthesis of (R)- and (S)-benzylglycidyl ether", Tetrahedron Letters, 1989, Vol. 30, No. 21, pages 2751-2754 See pages 2751, 2752.	7
X	WO 2017-031392 A1 (UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INCORPORATED) 23 February 2017 See claims 1-27; page 2, line 30-page 3, line 2; page 13, lines 1-9; and figure 1.	1-6
X	CAO, M. et al., "Composite fatty acid ether amides suppress growth of liver cancer cells in vitro and in an in vivo allograft mouse model", Cell Oncology, 2013, Vol. 36, pages 247-257 See abstract; page 248 and figure 1.	1-6
X	EP 0037780 A1 (PIERRE FABRE S.A.) 14 October 1981 See claim 1; and page 9, lines 1-19.	1-6

☐ Further documents are listed in the continuation of Box C.

☒ 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
"E" earlier application or patent but published on or after the international filing date
"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)
"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	Date of mailing of the international search report
14 March 2019 (14.03.2019)	**14 March 2019 (14.03.2019)**

Name and mailing address of the ISA/KR
International Application Division
Korean Intellectual Property Office
189 Cheongsa-ro, Seo-gu, Daejeon, 35208, Republic of Korea
Facsimile No. +82-42-481-8578

Authorized officer
LEE, Ki Cheul
Telephone No. +82-42-481-3353

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/043120

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.: 8-16
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 8-16 pertain to a method for treatment of the human by therapy, and thus relate to a subject matter which this International Searching Authority is not required, under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv), to search.

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 addtional 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 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2018/043120

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2011-0177108 A1	21/07/2011	CA 2733458 A1	11/02/2010
		EP 2313363 A2	27/04/2011
		JP 2011-530539 A	22/12/2011
		US 8871983 B2	28/10/2014
		WO 2010-017550 A2	11/02/2010
		WO 2010-017550 A3	20/05/2010
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EP 0037780 A1	14/10/1981	EP 0037780 B1	25/05/1983
		ES 8201531 A1	01/01/1982
		FR 2479813 A1	09/10/1981
		FR 2479813 B1	03/02/1984