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(54) Title: LIPID COMPOSITIONS AND THEIR USES FOR INTRATUMORAL POLYNUCLEOTIDE DELIVERY

(57) Abstract: The present application provides a composition comprising (1) a lipid composition comprising an ionizable amino lipid and a quaternary amine compound and (2) a polynucleotide. The present application also provides a composition comprising (1) a lipid composition comprising an asymmetric phospholipid, an ionizable amino lipid, and optionally a quaternary amine compound and (2) a polynucleotide, wherein the composition is formulated for intratumoral delivery of the polynucleotide. The present application further provides pharmaceutical compositions for intratumoral delivery comprising (1) a lipid composition comprising a compound of formula (I) and (2) therapeutic agent or a polynucleotide encoding the therapeutic agent, e.g., an mRNA encoding a therapeutic protein or a fragment thereof. Further provided is a method of increasing retention of a polynucleotide in a tumor tissue by using such a composition.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER INV. A61K47/44 ADD.		
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		
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) EPO-Internal, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2013/016058 A1 (MERCK SHARP & DOHME [US]; CAMERON MARK [US]; DAVIS JENNIFER R [US]; ST) 31 January 2013 (2013-01-31) page 24, line 18; compounds 6-30 -----	1-10
Y	WO 2013/052523 A1 (MODERNA THERAPEUTICS [US]; DE FOUGEROLLES ANTONIN [US]; ROY ATANU [US]) 11 April 2013 (2013-04-11) cited in the application claim 12 -----	1-10
Y	WO 2015/199952 A1 (ACUITAS THERAPEUTICS INC [CA]) 30 December 2015 (2015-12-30) cited in the application C-3 in reaction scheme 3 on page 50 ----- -/--	1-10
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" 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 "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	
30 August 2017	15/11/2017	
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Gettins, Marc	

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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:

see additional 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 an additional fees, this Authority did not invite payment of 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.:

1-10

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

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PCT/US2017/027492

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/086558 A1 (TEKMIRA PHARMACEUTICALS CORP [CA]; UNIV BRITISH COLUMBIA [CA]; ALNYLAM) 9 July 2009 (2009-07-09) page 1, line 24 - line 25; claim 3 -----	1-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2017/027492

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2013016058	A1	31-01-2013	NONE

WO 2013052523	A1	11-04-2013	AU 2012318752 A1 24-04-2014
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			EP 2224912 A1 08-09-2010
			EP 3100718 A1 07-12-2016
			JP 5749494 B2 15-07-2015
			JP 2011509258 A 24-03-2011
			JP 2014132014 A 17-07-2014
			US 2011117125 A1 19-05-2011
			WO 2009086558 A1 09-07-2009

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10

Compositions containing a lipid composition comprising an amino lipid, a quaternary amine compound and a polynucleotide

2. claims: 11-15

Composition for use (intratumoral delivery) comprising an amino lipid of formula (I) and a thereapeutic agent or a polynucleotide
