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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, 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,
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UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
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MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
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amendments (Rule 48.2(h))

- (88) **Date of publication of the international search report:**
9 April 2015

(54) **Title:** PHARMACEUTICAL COMPOSITIONS

(57) **Abstract:** The present invention relates to an ionic complex comprising a cationic polypeptide and an anionic excipient selected from: a PEG-carboxylic acid; a fatty acid having 10 or more carbon atoms; an anionic phospholipid; and a combination thereof. The invention also relates to a pharmaceutical composition comprising the ionic complex of the invention and a pharmaceutically acceptable carrier. The cationic polypeptide of the ionic complex has pharmacological activity and the complex can provide a more desirable pharmacokinetic profile for the cationic polypeptide of the complex as compared to the cationic polypeptide alone following administration. As such, the invention also relates to the use of the ionic complex and pharmaceutical composition comprising same to treat a subject suffering from a disease or disorder that is responsive to the cationic polypeptide of the ionic complex.



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A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K7/54 A61K38/12
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 C07K

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, BEILSTEIN Data, BIOSIS, WPI Data

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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

13 November 2014

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Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2014/029421

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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Y	----- BEDNAREK M A ET AL: "ANALOGS OF MTII, LACTAM DERIVATIVES OF ALPHA-MELANOTROPIN, MODIFIED AT THE N-TERMINUS, AND THEIR SELECTIVITY AT HUMAN MELANOCORTIN RECEPTORS 3, 4, AND 5", BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 261, no. 1, 1 January 1999 (1999-01-01), pages 209-213, XP002159223, ISSN: 0006-291X, DOI: 10.1006/BBRC.1999.0981 tables 1,2	16-25
Y	----- PAOLO GRIECO ET AL: "Structure-Activity Studies of the Melanocortin Peptides: Discovery of Potent and Selective Affinity Antagonists for the h MC3 and h MC4 Receptors +", JOURNAL OF MEDICINAL CHEMISTRY, vol. 45, no. 24, 1 November 2002 (2002-11-01), pages 5287-5294, XP055122990, ISSN: 0022-2623, DOI: 10.1021/jm0202526 Conclusions; figure 1; tables 1,2	16-25
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Y	----- US 5 731 408 A (HADLEY MAC E [US] ET AL) 24 March 1998 (1998-03-24) claims	16-25
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INTERNATIONAL SEARCH REPORT

International application No
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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.
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X	WO 2005/000339 A2 (LILLY CO ELI [US]; FLORA DAVID BENJAMIN [US]; HEIMAN MARK LOUIS [US];) 6 January 2005 (2005-01-06) -----	1,3,15, 16,18, 20-23, 39-56
Y	page 22, lines 3-11; claims 13,14; examples 9,16,17,28,123,124,140 -----	16-25
Y	WO 2005/014617 A2 (PALATIN TECHNOLOGIES INC [US]; SHARMA SHUBH D [US]; SHADIACK ANNETTE M) 17 February 2005 (2005-02-17) claims 27,59 -----	16-25
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Y	paragraph [06.3]; claims -----	16-25
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Y	WO 2010/144344 A2 (PALATIN TECHNOLOGIES INC [US]; SHI YI-QUN [US]; SHARMA SHUBH D [US]; D) 16 December 2010 (2010-12-16) page 50 - page 103; compounds -----	16-25
Y	WO 2011/060355 A1 (IPSEN PHARMA SAS [FR]; DONG ZHENG XIN [US]) 19 May 2011 (2011-05-19) claims -----	16-25
E	WO 2014/144260 A1 (RHYTHM METABOLIC INC [US]) 18 September 2014 (2014-09-18) claims ----- ----- -/--	1-25, 39-56

INTERNATIONAL SEARCH REPORT

International application No

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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.
X	VOGT T C B ET AL: "THE INTERACTIONS OF HISTIDINE-CONTAINING AMPHIPATHIC HELICAL PEPTIDE ANTIBIOTICS WITH LIPID BILAYERS THE EFFECTS OF CHARGES AND PH", JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, US, vol. 274, no. 41, 8 October 1999 (1999-10-08), pages 29115-29121, XP001053772, ISSN: 0021-9258, DOI: 10.1074/JBC.274.41.29115 abstract -----	1,5-7, 15,39, 40,43
X	WO 2007/022254 A2 (PRAECIS PHARM INC [US]; GEFTER MALCOLM L [US]; BARKER NICHOLAS [US]; M) 22 February 2007 (2007-02-22)	1,5-7, 15,39
Y	paragraph [0046]; claims -----	1-15
X	WO 94/26251 A1 (LIPOSOME TECHNOLOGY INC [US]) 24 November 1994 (1994-11-24)	1,5,6,9, 39
Y	page 10, lines 24-27; example 3 -----	1-15
X	WO 2009/158415 A1 (ENDO PHARMACEUTICALS SOLUTIONS [US]; KUZMA PETR [US]; DECKER STEFANIE) 30 December 2009 (2009-12-30)	1,3,4, 15,39
Y	paragraphs [0104], [0132]; claims -----	1-15
X	ZELIA MACEDO ET AL: "Biophysical Chemistry Estimation of average depth of penetration of melanotropins in dimyristoylphosphatidylglycerol vesicles", BIOPHYSICAL CHEMISTRY, vol. 59, 1 January 1996 (1996-01-01), pages 193-202, XP055151852, abstract; figures -----	1,5-7,39
X	WO 2012/172433 A2 (IPSEN PHARMA SAS [FR]; RICHARD JOEL [FR]; LAREDJ FAIZA [FR]; BARONNET) 20 December 2012 (2012-12-20) page 15, lines 16-27; claims; examples -----	1,5-7, 16-18, 20-25, 39,40, 43,44, 47-51,56

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. (means)

☒

 on paper

☒

 in electronic form
 - b. (time)

☐

 in the international application as filed

☐

 together with the international application in electronic form

☒

 subsequently to this Authority for the purpose of search
2.

☒

 In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

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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.:

24, 25(completely); 1-23, 39-56(partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 24, 25(completely); 1-23, 39-56(partially)

Compositions comprising a cationic peptide as defined in claims 24 and 25 and an anionic excipient as defined in claim 1.

2. claims: 26(completely); 1-23, 39-56(partially)

Compositions comprising a cationic peptide as defined in claim 26 and an anionic excipient as defined in claim 1.

3. claims: 27(completely); 1-23, 39-56(partially)

Compositions comprising a cationic peptide as defined in claim 27 and an anionic excipient as defined in claim 1.

4. claims: 28, 29(completely); 1-23, 39-51(partially)

Compositions comprising a cationic peptide as defined in claims 28 and 29 and an anionic excipient as defined in claim 1.

5. claims: 30(completely); 1-23, 39-56(partially)

Compositions comprising a cationic peptide as defined in claim 30 and an anionic excipient as defined in claim 1.

6. claims: 31, 32(completely); 1-23, 39-56(partially)

Compositions comprising a cationic peptide as defined in claims 31 and 32 and an anionic excipient as defined in claim 1.

- 7-11. claims: 33-37(completely); 1-23, 39-56(partially)

Compositions comprising a cationic peptide selected from one of claims 33-37 and an anionic excipient as defined in claim 1.

12. claims: 38(completely); 1-15, 39-56(partially)

Compositions comprising a cationic peptide as defined in claim 38 and an anionic excipient as defined in claim 1.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

13. claims: 1-15, 39-56(all partially)

Compositions comprising a cationic peptide not falling
within the scope of inventions 1-12 and an anionic excipient
as defined in claim 1.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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