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(54) Title: MU OPIOID RECEPTOR AGONIST ANALOGS OF THE ENDOMORPHINS

Tyr<-[D-Lys-Trp-Phe-Glu]-NH2
(SEQ ID NO 3)

C6H16N3O4
MW=752.3646

FIG. 1

(57) Abstract: The invention relates to cyclic peptide agonists that bind to the mu (morphine) opioid receptor and their use in the treatment of acute and/or chronic pain. Embodiments of the invention are directed to cyclic pentapeptide and hexapeptide analogs of endomorphin that have (i) a carboxy- terminal extension with an amidated hydrophilic amino acid and (ii) a substitution in amino acid position 2. These peptide analogs exhibited increased solubility compared to similar tetrapeptide analogs while maintaining favorable or improved therapeutic ratios of analgesia to side effects.
INTERNATIONAL SEARCH REPORT

International application No. PCT/US2011/043306

A. CLASSIFICATION OF SUBJECT MATTER

C07K 5/12(2006.01)i, C07K 7/64(2006.01)i, A61K 38/12(2006.01)i, G01N 33/68(2006.01)i, A61P 1/12(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)
C07K 5/12; A61K 38/08; A61K 38/12; A61K 31/44; A61K 31/53

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 database consulted during the international search (name of database and, where practical, search terms used)
eKOMPASS/KIPO internal, Google & Keywords: cyclic peptide, mu, opioid, receptor, etc.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tr>
<td>A</td>
<td>US 05872097 A (FROLENHAG, K. I., et al.) 16 February 1999 See the whole document.</td>
<td>1-10,17-27</td>
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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 citation or other special reason (as specified)
  "O" document referring to an oral disclosure, use, exhibition or other means
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  "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
  "R" document member of the same patent family

Date of the actual completion of the international search
27 MARCH 2012 (27.03.2012)

Date of mailing of the international search report
28 MARCH 2012 (28.03.2012)

Name and mailing address of the ISA/KR
Korean Intellectual Property Office
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Facsimile No. 82-42-472-7140

Authorized officer
AHN, Kyu Jeong
Telephone No. 82-42-481-5975

Form PCT/ISA/210 (second sheet) (July 2009)
## INTERNATIONAL SEARCH REPORT

### 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.: 11-16**
   - Because they relate to subject matter not required to be searched by this Authority, namely:
     - Claims 11-16 are directed to methods for treatment of the human body by therapy, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, 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. **Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

2. **As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.**

3. **As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.**

4. **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.:**

5. **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.

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2009)
<table>
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