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- (81) **Designated States (unless otherwise indicated, for every kind of national protection available):** AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, 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, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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15 September 2011

(54) **Title:** FORMULATIONS OF GUANYLATE CYCLASE C AGONISTS AND METHODS OF USE

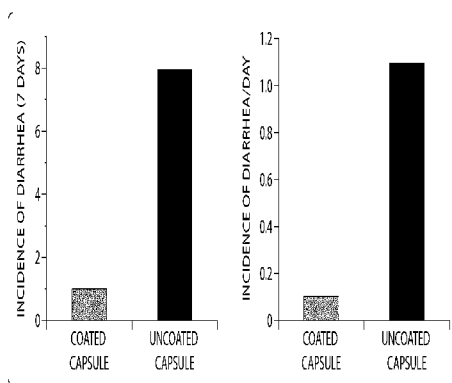


Fig. 22

(57) **Abstract:** The invention provides novel formulations of guanylate cyclase-C ("GCC") agonist peptides and methods for their use in the treatment of gastrointestinal diseases and disorders, including gastrointestinal cancer. The GCC agonist formulations of the invention can be administered either alone or in combination with one or more additional therapeutic agents, preferably an inhibitor of cGMP-dependent phosphodiesterase or a laxative.

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/48 A61K38/00
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 practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, WPI Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/137318 A1 (IRONWOOD PHARMACEUTICALS INC [US]; CURRIE MARK G [US]; ZIMMER DANIEL P) 13 November 2008 (2008-11-13) peptide 10; page 34 - page 80; claims -----	1-39
X	WO 2006/086653 A2 (MICROBIA INC [US]; CURRIE MARK G [US]; MAHAJAN-MIKLOS SHALINA [US]; SU) 17 August 2006 (2006-08-17) Peptide 20; page 65 - page 94; claims; sequences -----	1-39
E	WO 2009/149279 A2 (SYNERGY PHARMACEUTICALS INC [US]; SHAILUBHAI KUNWAR [US]; JACOB GRAY S) 10 December 2009 (2009-12-10) claims; sequence 1 ----- -/--	1-39

☒ 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 document 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

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Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2009/066600

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 2009/149278 A1 (SYNERGY PHARMACEUTICALS INC [US]; SHAILUBHAI KUNWAR [US]; JACOB GARY S) 10 December 2009 (2009-12-10) the whole document -----	1-39
X,P	WO 2008/151257 A2 (SYNERGY PHARMACEUTICALS INC [US]; SHAILUBHAI KUNWAR [US]; JACOB GARY S) 11 December 2008 (2008-12-11) page 21 - page 82; claims; figures; sequences -----	1-10, 13-15, 19,20, 25-39
X	WO 2005/016244 A2 (MICROBIA INC [US]; CURRIE MARK G [US]; MAHAJAN-MIKLOS SHALINA [US]; LI) 24 February 2005 (2005-02-24) peptide 17 -----	1-4,19, 20,25
X	WO 02/078683 A1 (SYNERGY PHARMACEUTICALS INC [US]) 10 October 2002 (2002-10-10) sequence 20 -----	1-4,25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/066600

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.:

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

International Application No. PCT/ US2009/ 066600

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-24(partially)

A GCC agonist formulation comprising a core containing one GCC agonist peptide of SEQ. ID. NO: 1 and one or more targeting materials.

2-7. claims: 1, 4-24(all partially)

As invention 1 but referring to SEQ. ID. NO: 2-7, respectively.

8. claims: 1, 2, 4-24(all partially)

As invention 1 but referring to SEQ. ID. NO: 8

9. claims: 1-24(partially)

As invention 1 but referring to SEQ. ID. NO: 9

10-54. claims: 1, 4-24(all partially)

As invention 1 but referring to SEQ. ID. NO: 10-54, respectively.

55-56. claims: 1, 2, 4-24(all partially)

As invention 1 but referring to SEQ. ID. NO: 55 and 56, respectively.

57-249. claims: 1, 4-24(all partially)

As invention 1 but referring to SEQ. ID. NO: 57-249, respectively.

250. claims: 25-39(partially)

A method for treating or preventing gastrointestinal disorders by administering GCC agonist formulation comprising a core containing one GCC agonist peptide of SEQ. ID. NO: 1 and one or more targeting materials.

251-256. claims: 25-31, 34-39(all partially)

As invention 250, but referring to SEQ. ID. NO:2-7

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US2009/ 066600

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

257. claims: 25-32, 34-39(all partially)

As invention 250 but referring to SEQ. ID. NO: 8

258. claims: 25-39(partially)

As invention 250 but referring to SEQ. ID. NO: 9

259-303. claims: 25-31, 34-39(all partially)

As invention 250 but referring to SEQ. ID. NO: 10-54,
respectively.

304-305. claims: 25-32, 34-39(all partially)

As invention 250 but referring to SEQ. ID. NO: 55 and 56,
respectively.

306-498. claims: 25-31, 34-39(all partially)

As invention 250 but referring to SEQ. ID. NO: 57-249,
respectively.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2009/066600

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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