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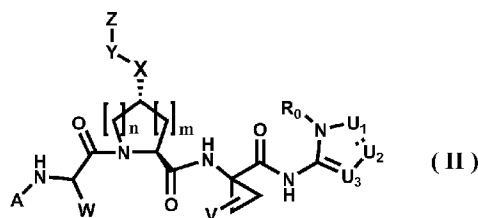
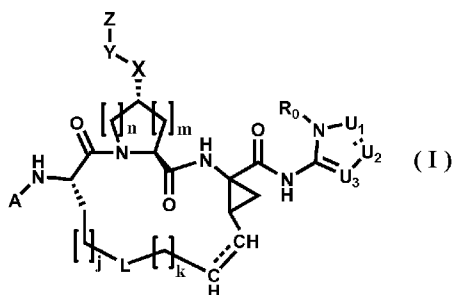
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(54) Title: ACYLAMINOHETEROARYL HEPATITIS C VIRUS PROTEASE INHIBITORS



(57) Abstract: The present invention discloses compounds of formulae (I) and (II), or pharmaceutically acceptable salts, esters, or prodrugs thereof: Which inhibit serine protease activity, particularly the activity of hepatitis C virus (HCV) NS3-NS4A protease. Consequently, the compounds of the present invention interfere with the life cycle of the hepatitis C virus and are also useful as antiviral agents. The present invention further relates to pharmaceutical compositions comprising the aforementioned compounds for administration to a subject suffering from HCV infection. The invention also relates to methods of treating an HCV infection in a subject by administering to the subject a pharmaceutical composition comprising a compound of the present invention.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/75580

A. CLASSIFICATION OF SUBJECT MATTER

IPC: **A61K 38/12** (2006.01)

USPC: 514/11

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)

U.S. : 514/11

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)
STN (registry, zcap) structure of cyclic compounds of formula (I)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6,323,180 (LINAS-BRUNET et al) 27 November 2001 (27.11.2001), throughout	1
A	US 7,041,698 (RIPKA et al) 09 May 2006 (09.05.2006) throughout	1

☐

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 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

29 August 2008 (29.08.2008)

Date of mailing of the international search report

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Name and mailing address of the ISA/US

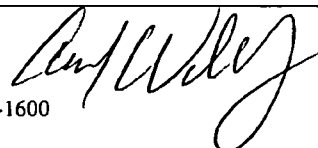
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/75580

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:
Please See Continuation 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 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.: 1-8 and 10-20 (cyclic compounds)
- 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/US07/75580

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This International Search Authority has found 2 inventions claimed in the International Application covered by the claims indicated below. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-8 and 10-20, drawn to cyclic HCV inhibitors of general formula (I).

Group II, claim(s) 1-7 and 9-20, drawn to linear HCV inhibitors of general formula (II).

1. This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

According to PCT Rule 13.2, unity of invention exists only when there is a shared same or corresponding special technical feature among the claimed inventions. The technical feature of Group I is the cyclic inhibitor while the technical feature of Group II is being a linear inhibitor. The elements of W and V in Group II cannot, and do not, form the cyclizing moiety of Group I.

Furthermore, Annex B, Part I(f) of the Administrative Instructions under PCT states that, "wherein a single claim defines alternatives (chemical or non-chemical)...the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature."

The alternatives must comply with subsections (i)(A) and one of either (i)(B)(1) or (i)(B)(2), which requires that, "all alternatives have a common property or activity" and "a common structure is present i.e., a significant structural element is shared by all of the alternatives" (B)(1) or "in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains." (B)(2).

In the instant case, the method requires that the compounds have the same activity/function (HCV inhibitors), satisfying requirement (A). However, the claim fails to satisfy either (B)(1) or (B)(2). The claim recites no common corestructure essential for the function, thus failing to meet the requirements of (B)(1), as many of the positions are variable and can have vastly divergent elements. Furthermore, as discussed above, the two compounds are structurally divergent, one being cyclic, the other being linear, where the linear compound does not, and cannot, embrace the cyclic compound.

Further, in looking to subsection (f)(iii), it is stated that 'recognized class of chemical compounds' means that, "there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved." One of skill in the art would not recognize these divergent compounds, or other compounds asserted to have said activity/function, as required, to function in the context of the instantly claimed invention. Thus, the claim fails to meet the requirement of (B)(2).