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C07D 405/12 (2006.01)	*C07D 487/10* (2006.01)
C07D 413/12 (2006.01)	*C07D 491/107* (2006.01)
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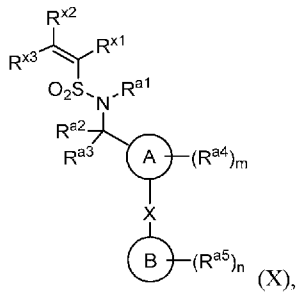
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(54) Title: K-RAS MODULATORS WITH A VINYL SULFONAMIDE MOIETY



(X),

(57) Abstract: Provided herein are compounds comprising a vinyl sulfonamide moiety. Also provided herein are pharmaceutical compositions comprising such compounds, and methods of using such compounds and pharmaceutical compositions for inhibiting the post-translational processing of K-Ras precursors, and for treating disorders such as cancer.

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[Continued on next page]

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) Date of publication of the international search report:
28 November 2019 (28.11.2019)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/027959

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D403/12 C07D401/14 C07D491/08 C07D401/12 C07D405/12
C07D413/12 C07D417/12 C07D471/08 C07D487/08 A61P35/00
A61K31/40 A61K31/445 C07D487/10 C07D491/107 C07D207/48

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)
C07D A61P

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.
X	WO 2016/179558 A1 (UNIV CALIFORNIA [US]; LEIDOS BIOMEDICAL RES INC [US]) 10 November 2016 (2016-11-10)	1-47, 49-56, 61-82
A	claims 1, 40, 41 paragraph [0263] - paragraph [0267] paragraph [0549]; claim 26	57-60
X	US 2014/288045 A1 (REN PINGDA [US] ET AL) 25 September 2014 (2014-09-25)	1-47, 49-56, 61-82
A	claim 1; examples 25, 58	57-60

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[X] Further documents are listed in the continuation of Box C.

[X] 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
1 October 2019	22/10/2019

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Miniejew, Catherine

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 4 November 2008 (2008-11-04), XP002792949, retrieved from STN Database accession no. 1070688-79-7 abstract	1,2,5, 10,11, 13,14, 20-23, 41,45, 46,50

X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2 November 2008 (2008-11-02), XP002792950, retrieved from STN Database accession no. 1069483-13-1 abstract	1,2,5, 10,11, 13,14, 20-23, 41,45, 46,50

X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 27 May 2004 (2004-05-27), XP002792951, retrieved from STN Database accession no. 686272-37-7	1,2,11, 13,15, 20-23, 41,45, 46,50
A	abstract	57-60

X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 3 November 2008 (2008-11-03), XP002792952, retrieved from STN Database accession no. 1069948-57-7 abstract	1,2,5, 10,11, 13,14, 19-23, 27,28, 41,45, 46,50

X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 10 August 2010 (2010-08-10), XP002792953, retrieved from STN Database accession no. 1235624-64-2 abstract	1,2,11, 13,41, 45,46,50

X	WO 2005/073198 A1 (WYETH CORP [US]; RESNICK LYNN [US] ET AL.) 11 August 2005 (2005-08-11) claim 1; table 3; compound 9	1,12,18, 19,46, 49,50, 52,61

A	WO 2014/152588 A1 (ARAXES PHARMA LLC [US]) 25 September 2014 (2014-09-25) claims 1, 122, 123; examples	1-47, 49-82

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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	WO 2007/060215 A2 (DOMPE SPA [IT]; ALLEGRETTI MARCELLO [IT] ET AL.) 31 May 2007 (2007-05-31) claim 1; example 2A	1,18,47, 50,52,55
X	WO 2008/075070 A1 (ASTRAZENECA AB [SE]; ASTRAZENECA UK LTD [GB] ET AL.) 26 June 2008 (2008-06-26) claim 1; examples 98, 104	1,13,14, 45,47, 49,54, 55,61
X	US 3 526 638 A (HROMATKA OTTO ET AL) 1 September 1970 (1970-09-01) example 1(a)	1,18,45, 47,50, 52,54,55
X	WO 2017/066193 A1 (PRINCETON DRUG DISCOVERY LLC [US]) 20 April 2017 (2017-04-20) example 3 scheme 3; page 38 claim 1	1,13,15, 45,47, 49,50, 54,55,61

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/027959

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.: 48(completely); 1-47, 49-56, 61-82(partially)
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:
see FURTHER INFORMATION sheet PCT/ISA/210

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.:

46, 47, 57-60(completely); 1-45, 49-56, 61-82(partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 46, 57(completely); 1-45, 49-56, 58-82(partially)

   subject-matter related to the compounds of formula (X) when X is -S(O)-, -S(O)2-, -S(O)NRa46

   ---

2. claims: 1-45, 49-56, 61-82(all partially)

   subject-matter related to the compounds of formula (X) when X is -C(S)-

   ---

3. claims: 47(completely); 1-45, 49-56, 58-82(partially)

   subject-matter related to the compounds of formula (X) when X is -C(O)-

   ---

4. claims: 48(completely); 1-45, 49-56, 61-82(partially)

   subject-matter related to the compounds of formula (X) when X is -C(Ra6)2-

   ---

Continuation of Box II.2

Claims Nos.: 48(completely); 1-47, 49-56, 61-82(partially)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty of invention-1 and invention-3. So many documents were retrieved that it is impossible to determine which parts of invention-1 and invention-3 may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). At least, D3-D8 are anticipating the subject-matter of invention-1 when Rx1 and Rx2 together form a ring and at least D1, D2, D10-D13 anticipate the subject-matter of invention-3 (see passages cited in the international search report). It appears that in none of the tested examples of invention-1 and invention-3 Rx1 and Rx2 together form a ring. For these reasons, the search was performed taking into consideration the non-compliance in determining the extent of the search and the search of invention-1 and invention-3 has been restricted to the subject-matter related to the compounds of formula (X) wherein Rx1 and Rx2 together do not form a ring.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2019/027959

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

Information on patent family members

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