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(54) Title: INHIBITION OF SHP2/PTPN1 1 PROTEIN TYROSINE PHOSPHATASE BY NSC-87877, NSC-1 17199 AND THEIR ANALOGS

(57) Abstract: Compounds and associated methods for inhibiting a protein tyrosine phosphatase. By a combination of experimental and virtual screenings of the NCI Diversity Set chemical library, NSC-87877 and NSC-1 17199 have been identified as Shp2 PTP inhibitors. Significantly, NSC-87877 is active in cell-based assays and has no detectable off-target effects in the EGF-stimulated Erk1/2 activation pathway. Additionally, a number of analogs of NSC-1 17199 have been produced. These analogs exhibit enhanced protein tyrosine phosphatase inhibition and are found to be potent and/or selective inhibitors of Shp 1 and/or Shp2 protein tyrosine phosphatases.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/08876

A. CLASSIFICATION OF SUBJECT MATTER

IPC: A01N 43/00(2006.01);A61K 31/33(2006.01)

USPC: 514/183

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. : 514/183

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: structure search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2005/0209301 A1 (Eissenstat et al.) 22 Sept. 2005 (22.09.05), entire document	1-17
A	US 2004/0204458 A1 (Roth et al.) 14 October 2004 (14.10.04), entire document	1-17



Further documents are listed in the continuation of Box C.

D

See patent family annex.

* Special categories of cited documents	"T"
"A" document defining the general state of the art which is not considered to be of particular relevance	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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

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INTERNATIONAL SEARCH REPORT

PCT/US07/08876

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:

- I. ☐ 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:

A written lack of unity of invention was mailed on March 26, 2008 and no response has been received. A call was placed to the attorney on record, but it was not returned. Thus only group I (claims 1-17) will be searched.

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.: 1-17

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/US07/08876

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

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Box No. UI Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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