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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:

13 December 2012

(54) Title: METHODS FOR INHIBITING VIRUS REPLICATION

(57) Abstract: The present invention provides methods for treating a subject having, or at risk of having, a viral infection. The methods include, but are not limited to, the use of 4-(dipropylsulfamoyl) benzoic acid, an inhibitor of CDC25B phosphatase, an inhibitor of ICAM-1, an inhibitor of CamK2B, or a combination thereof.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/33631

A. CLASSIFICATION OF SUBJECT MATTER
 IPC(8) - A61K 31/18, 31/10, 31/045 (2012.01)
 USPC - 514/604, 709, 730

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)

IPC(8) - A61K 31/18, 31/10, 31/045 (2012.01)

USPC - 514/604, 709, 730

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 514/579, 601, 602, 706, 708, 724, 762, 764

(Text Search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST (PGPB, USPT, USOC, EPAB, JPAB); PatBase and Google Scholar.

Search Terms: 4-(dipropylsulfamoyl) benzoic acid, 4-(dipropylsulfamoyl)benzoic acid, probenecid, influenza, viral, virus, carbon, substitut\$, halogen, nitrile, nitrite, hydroxy, alkoxy, nitrate, sulfate, amino, nitro, sulfonate, alky, variant, derivative, analog, NSC95397, CamK2B

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	US 2011/0038852 A1 (MELDRUM et al.) 17 February 2011 (17.02.2011) abstract; para [0005], [0165], [0224], [0270]	1 ----- 5 and 8
Y	KONIG, et al. "Human host factors required for influenza virus replication" Nature; 11 February 2010; Vol. 463; pages 813-817: abstract; pg 817, col 1, para 1	5
Y	ISRAILI et al. "Metabolites of Probenecid. Chemical, Physical, and Pharmacological Studies"; J. Med. Chem.; 1972; Vol. 15, No 7; pages 709-713: Abstract; pg 709, col 2, para 1; pg 710, col 1, para 4; pg 712, col 2, para 4 to pg 713, col 1, para 3	8
A	US 2006/0233743 A1 (KELLY) 19 October 2006 (19.10.2006) claim 38; para [0218]-[0223].	1

☐ Further documents are listed in the continuation of Box C.

* 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

03 October 2012 (03.10.2012)

Date of mailing of the international search report

23 OCT 2012

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/33631

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.: 9-14, 17 and 18
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:

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: claims 1, 5 and 8, directed to a method for treating a subject comprising: administering to a subject an effective amount of a composition comprising 4-(dipropylsulfamoyl)benzoic acid, wherein the subject has or is at risk of having an influenza virus infection, wherein the subject comprises no greater than a detectable level of oseltamivir carboxylate.

Group II: claims 2, 5, 8, 15 and 16 directed to a method for treating a subject comprising: administering to a subject an effective amount of a composition comprising 4-(dipropylsulfamoyl)benzoic acid, wherein the subject has or is at risk of having a virus infection, wherein the virus infection is not an influenza virus infection.

- Please see extra sheet for continuation -

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 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, 5, and 8

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/US 12/33631

Continuation of Box III: Lack of Unity of Invention

Group III: claims 3, 6, 8, 15, 16, 19 and 20, directed to a method for treating a subject comprising: administering to a subject an effective amount of a composition comprising an inhibitor of CDC25B phosphatase, wherein the subject has or is at risk of having a virus infection.

Group IV: claims 4, 7, 8, 15, 16, 21 and 22, directed to a method for treating a subject comprising: administering to a subject an effective amount of a composition comprising an inhibitor of ICAM-1, wherein the subject has or is at risk of having a virus infection,

The inventions listed as Groups I - IV 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:

The special technical feature of the claims of Groups I-IV are disclosed in the Group descriptions, above. It should be noted that, while some dependent claims in each Group may further combine additional active agents for the treatments of each Group, each Group is not limited to said combinations.

The only common technical element shared by the above groups is that they are related to treatment of viral infections by administration of an effective amount of an agent to a subject. Groups I and II share the further common technical element of being related to at least administration of 4-(dipropylsulfamoyl)benzoic acid (probenicid). These common technical elements do not represent an improvement over the prior art of US 2006/0233743 A1 to Kelly, which teaches anti-viral treatment (para [0218]-[0223]), comprising administering to a subject an effective amount of a composition (abstract) comprising 4-(dipropylsulfamoyl)benzoic acid (probenicid)(claim 38), wherein the subject has or is at risk of having a viral infection (para [0218]-[0223]).

Therefore, the inventions of Groups I-IV lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.