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(54) Title: THERAPEUTIC COMPOSITIONS AND METHODS FOR TREATING HEPATITIS B

(57) Abstract: The invention provides therapeutic combinations and therapeutic methods that are useful for treating Hepatitis B.



WO 2017/120527 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US17/12614

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 39/12, 39/29; C07K 14/01, 14/02; C12N 15/51 (2017.01)

CPC - A61K 39/12, 39/292; C07K 14/01, 14/02

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)

See Search History document

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

See Search History document

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2015/172128 A1 (INDIANA UNIVERSITY RESEARCH AND TECHNOLOGY CORPORATION et al.) 12 November 2015; paragraphs [0009], [0029]-[0030], [0032]-[0033], [0078], [0085]; claims 1-3, 7	1-3, 4/1-3, 5/4/1-3, 16, 18, 21/18, 22/21/18, 33, 35, 38/35, 39/38/35, 53
Y	(STRAY, SJ et al.) BAY 41-4109 has Multiple Effects on Hepatitis B Virus Capsid Assembly. Journal of Molecular Recognition. 27 September 2006; Vol. 19, No.6; pages 542-548; abstract; page 544, column 2, paragraph 3	1-3, 4/1-3, 5/4/1-3, 16, 18, 21/18, 22/21/18, 33, 35, 38/35, 39/38/35, 53
Y	US 2011/0218512 A1 (TULLIS, RH et al.) 08 September 2011; abstract; paragraph [0016]	18, 21/18, 22/21/28, 33
A	US 6,809,083 B1 (MUELLER, RA et al.) 26 October 2004; whole document	1-3, 4/1-3, 5/4/1-3, 16, 35, 38/35, 39/38/35, 53

☐ 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 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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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US17/12614

Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
- a. ☐ forming part of the international application as filed:
☐ in the form of an Annex C/ST.25 text file.
☐ on paper or in the form of an image file.
- b. ☐ furnished together with the international application under PCT Rule 13*ter*. 1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
- c. ☒ furnished subsequent to the international filing date for the purposes of international search only:
☒ in the form of an Annex C/ST.25 text file (Rule 13*ter*. 1(a)).
☐ on paper or in the form of an image file (Rule 13*ter*. 1(b) and Administrative Instructions, Section 713).
2. ☒ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US17/12614

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.: 6-15, 23-32, 40-52, 55
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 Supplemental Page-*****

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.:
Groups I+, claims 1 (in-part), 2 (in-part), 3 (in-part), 4 (in-part), 5 (in-part), 16 (in-part), 18 (in-part), 21 (in-part), 22 (in-part), 33 (in-part), 35 (in-part), 38 (in-part), 39 (in-part) and 53 (in-part)

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
Information on patent family members

International application No.
PCT/US17/12614

-***-Continued from Box No. III: Observations where unity of invention is lacking-***-

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.

Groups I+, Claims 1-5, 16-22, 33-39, 53, 54; a capsid inhibitor and a sAg secretion inhibitor are directed toward a method for treating hepatitis B in an animal, comprising administering to the animal at least two agents selected from the group consisting of: a) reverse transcriptase inhibitors; b) capsid inhibitors; c) cccDNA formation inhibitors; d) sAg secretion inhibitors; e) oligomeric nucleotides targeted to the Hepatitis B genome; and f) immunostimulators; and a composition and kit therefor.

The method, composition and kit will be searched to the extent they encompass a capsid inhibitor (first exemplary agent), and a surface antigen (sAg) secretion inhibitor (second exemplary agent). Applicant is invited to elect additional agent(s), or classes thereof, to be searched. Additional agent(s) will be searched upon the payment of additional fees. It is believed that claims 1 (in-part), 2 (in-part), 3 (in-part), 4 (in-part), 5 (in-part), 16 (in-part), 18 (in-part), 21 (in-part), 22 (in-part), 33 (in-part), 35 (in-part), 38 (in-part), 39 (in-part) and 53 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass a capsid inhibitor (agent), and a surface antigen (sAg) secretion inhibitor (agent). Applicants must specify the claims that encompass any additionally elected agent(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be an agent encompassing a reverse transcriptase inhibitor (first exemplary elected agent).

No technical features are shared between the agents of Groups I+ and, accordingly, these groups lack unity a priori.

Groups I+ share the technical features including: a method for treating hepatitis B in an animal comprising administering to the animal at least two agents selected from the group consisting of: a) capsid inhibitors; b) sAg secretion inhibitors; c) reverse transcriptase inhibitors; d) cccDNA formation inhibitors; e) oligomeric nucleotides targeted to the Hepatitis B genome; and f) immunostimulators; a pharmaceutical composition that comprises a pharmaceutically acceptable carrier and at least said two agents; and a kit comprising at least said two agents.

However, these shared technical features are previously disclosed by US 6,809,083 B1 to Mueller et al. (hereinafter 'Mueller').

Mueller discloses a method for treating hepatitis B in an animal (a method for treating hepatitis B in a mammal (an animal); abstract, column 3, lines 18-21) comprising administering to the animal at least two agents (comprising administering to the mammal (animal) at least two agents; abstract, column 3, lines 18-21, column 4, lines 28-39) including reverse transcriptase inhibitors (a nucleoside or nucleotide antiviral compound (reverse transcriptase inhibitor); column 2, lines 39-55; column 4, lines 28-39) and immunostimulators (and immunostimulators; column 4, line 36); a pharmaceutical composition that comprises a pharmaceutically acceptable carrier and at least said two agents (a pharmaceutical composition that comprises a pharmaceutically acceptable carrier and at least said two agents; column 4, lines 28-39, column 5, lines 23-30); and a kit comprising at least said two agents.

Mueller does not disclose: a kit comprising at least said two agents. However, It would have been obvious to a person of ordinary skill in the art at the time of the invention was made to have modified the disclosure of Mueller to have provided the at least two agents, as disclosed by Mueller, or a composition comprising said agents, as disclosed by Mueller, in a kit with instructions for use to perform a method of treatment of an animal for HBV, as disclosed by Mueller, in order to more readily and easily enable a medical practitioner to determine appropriate doses of the agents, and to administer the agents to said animal.

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Mueller reference, unity of invention is lacking.