Abstract:

A 61K 31/445 (2006.01)  

4.1 Dengue virus and/or a virus belonging to the Orthomyxoviridae family, such as an Influenza A virus.

Figure 1

Figure 1

UV-12 100 mg/kg
UV-12 4 g/kg
UV-28 100 mg/kg
UV-28 40 mg/kg
Vehicle

Title: DEOXYNOJIRIMYCIN DERIVATIVES AND METHODS OF THEIR USING

(57) Abstract: The present application provide novel iminosugars and their use in treatment of viral infections, such as Dengue infection and Influenza A infection. The present inventors discovered certain deoxynojirimycin derivatives may be effective against one or more viruses, which may be, for example, a Dengue virus and/or a virus belonging to the Orthomyxoviridae family, such as an Influenza A virus. In particular, such deoxynojirimycin derivatives may be useful for treating a disease or condition caused by or associated with one or more viruses. In certain embodiments, the deoxynojirimycin derivatives may increase a survival rate or probability for a subject infected with one or more viruses, which may be, for example, a Dengue virus and/or a virus belonging to the Orthomyxoviridae family, such as an Influenza A virus.
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: 7 May 2015
A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 31/445 (2015.01)
CPC - A61K 31/445 (2014.1.1)

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 31/445; A61P 31/12 (2015.01)
CPC - A61K 31/445, 31/453 (2014.1.1) (keyword delimited)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 514/315, 326, 328; 546/219 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase, STN, Google Patents, Google Scholar, PubChem
Search terms used: n-nonyl-deoxynojirimycin THF dimethyl methoxy piperidine

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>US 201 10189771 A1 (BLOCK et al) 04 August 2001 (04.08.2001) entire document</td>
<td>1-19</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C.

Date of the actual completion of the international search
05 February 2015

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
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Authorized officer: Blaine R. Copenheaver
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Form PCT/ISA/210 (second sheet) (July 2009)
### INTERNATIONAL SEARCH REPORT

**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.:<br>because they relate to subject matter not required to be searched by this Authority, namely:

2. **☐** Claims Nos.:<br>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.:<br>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:

Claims 1, 2, 5-7, 9-15, 18, and 19 have been analyzed subject to the restriction that the claims read on the formula (I) as described in the Lack of Unity of Invention (See Extra Sheet). The claims are restricted to compound of formula (I); or a pharmaceutically acceptable salt thereof wherein W1-W4 are each independently hydrogen; R1 is a C1 alkyl group; R2 and R3 are each independently hydrogen; a pharmaceutical composition thereof; and methods thereof.

<See Extra 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 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.: 1-19 as they read on the elected species (See Extra Sheet)

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.

Form PCT/ISA/2 10 (continuation of first sheet (2)) (July 2009)
INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/055599

Claims 1-3, 5-16, 18, and 19 have been analyzed subject to the restriction that the claims read on the formula (I) as described as compound 1) in the Response to the Invitation to Pay Additional Fees in the International Application dated 23 December 2014. The claims are restricted to a compound of formula (I); or a pharmaceutically acceptable salt thereof wherein W1-4 each being H; R1 being H; R2 and R3 being together -CH2-CH2-; a pharmaceutical composition thereof; and methods thereof.

Claims 1, 2, 4-7, 9-15, and 17-19 have been analyzed subject to the restriction that the claims read on the formula (I) as described as compound 2) in the Response to the Invitation to Pay Additional Fees in the International Application dated 23 December 2014. The claims are restricted to a compound of formula (I); or a pharmaceutically acceptable salt thereof wherein W1-4 each being H; R1 and R2 each being CH3; R3 being H; a pharmaceutical composition thereof; and methods thereof.

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 need to be paid.

Group I: Claims 1-19 are drawn to a compound of formula (I); or a pharmaceutically acceptable salt thereof, a pharmaceutical composition thereof, and methods thereof.

The first invention of Group I is restricted based on the proviso that at least one of R1-3 is not hydrogen and is restricted to a compound of formula (I); or a pharmaceutically acceptable salt thereof wherein W1-4 are each independently hydrogen; R1 is a C1 alkyl group; R2 and R3 are each independently hydrogen; a pharmaceutical composition thereof; and methods thereof. It is believed that claims 1, 2, 5-7, 9-15, 18 and 19 read on this first named invention and thus these claims will be searched without fee to the extent that they read on the above embodiment.

Applicant is invited to elect additional formula(e) for each additional compound to be searched in a specific combination by paying an additional fee for each set of election. An exemplary election would be a compound of formula (I); or a pharmaceutically acceptable salt thereof wherein W1 is a C1 alkyl group; W2-4 are each independently hydrogen; R1 is a C1 alkyl group; R2 and R3 are each independently hydrogen; a pharmaceutical composition thereof; and methods thereof. Additional formula(e) will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on 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.

The inventions listed in Groups I 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 Groups I formulae do not share a significant structural element, requiring the selection of alternatives for the compound variables W1, W2, W3, W4, R1, R2, and R3.

The Groups I share the technical features of a compound comprising the core structure of formula (I); or a pharmaceutically acceptable salt thereof; a pharmaceutical composition comprising a) a pharmaceutically acceptable amount of the compound comprising the core structure of formula (I) and b) a pharmaceutically acceptable carrier; a method of treating or preventing a Dengue viral infection comprising administering to a subject in need thereof the compound comprising the core structure of formula (I); or a pharmaceutically acceptable salt thereof; and a method of treating a disease or condition caused by or associated with a virus belonging to the Orthomyxoviridae family comprising administering to a subject in need thereof the compound comprising the core structure of formula (I); or a pharmaceutically acceptable salt thereof. However, these shared technical features do not represent a contribution over the prior art.

Specifically, "Synthesis and a-amylase inhibitory activity of glucose-deoxyribozyme conjugates" to Kato et al. teach a compound comprising the core structure of formula (I); or a pharmaceutically acceptable salt thereof wherein W1-4 are each independently hydrogen; R1 and R2 are each independently hydrogen (See Pg. 7693, Scheme 1, compound 8b;...-shown structure...; Pg. 7697, Col. 1, 4th para. 4.2.5.2 4-0-[9-[(2R, 3R, 4R, 5S)3,4,5-trihydroxy-2-hydroxy(2-methylpiperidino)nonyl]-D-glucopyranose, (8b)).

Additionally, US 2011/0189771 A1 to Block et al. teach a compound similar to the compound of formula (I) (Abstract; Claim 4; Para. [0009]), and a pharmaceutical composition comprising a) a pharmaceutically acceptable amount of a compound and b) a pharmaceutically acceptable carrier (See Para. [0036]; Para. [0003]); a method of treating or preventing a Dengue viral infection comprising administering to a subject in need thereof a compound or a pharmaceutically acceptable salt thereof (Para. [0003]; Para. [0016]; Para. [0030], Table 2); and a method of treating a disease or condition caused by or associated with a virus belonging to the Orthomyxoviridae family comprising administering to a subject in need thereof a compound or a pharmaceutically acceptable salt thereof (Para. [0003]; Para. [0005]).

The inventions listed in Groups I therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.