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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))

(88) Date of publication of the international search report:

25 April 2019 (25.04.2019)

(54) Title: COMPOSITIONS AND METHODS FOR THE DELIVERY OF THERAPEUTICS

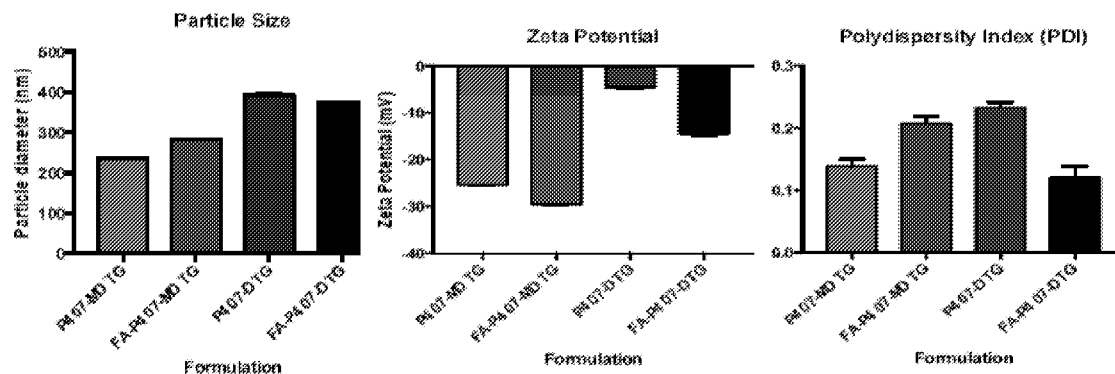


Figure 1

(57) Abstract: The present invention provides compositions and methods for the delivery of antivirals to a cell or subject.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2017/038693

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07D 498/14; A61K 31/4985; A61K 31/5365; C07D 487/14 (2017.01)

CPC - C07D 498/14; A61K 31/4985; A61K 31/5365; C07D 487/14 (2017.08)

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

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.
A	US 2014/0221378 A1 (JAPAN TOBACCO INC) 07 August 2014 (07.08.2014) entire document	1, 9-29
A	US 2013/0171214 A1 (VIIV HEALTHCARE COMPANY) 04 July 2013 (04.07.2013) entire document	1, 9-29
A	US 2015/0232479 A1 (SHIONOGI & CO LTD et al) 20 August 2015 (20.08.2015) entire document	1, 9-29
A	US 2014/0011995 A1 (SUMINO et al) 09 January 2014 (09.01.2014) entire document	1, 9-29



Further documents are listed in the continuation of Box C.



See patent family annex.

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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

06 November 2017

Date of mailing of the international search report

27 NOV 2017

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2017/038693

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.:
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 Extra Sheet

Claims 1 and 9-29 have been analyzed subject to the restriction that the claims read on a prodrug compound of the formula I-A and pharmaceutically acceptable salts thereof wherein ring A is (II-A), the stereochemistry of an asymmetric carbon represented by * has R-configuration; m is 0; R is (L)n-R1; L is absent; n is 0; R1 is H; nanoparticles thereof; pharmaceutical compositions thereof; methods of treating, inhibiting, or preventing an HIV infection in a subject.

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, 9-29

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/US2017/038693

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 need to be paid.

Group I+: claims 1-29 are drawn to prodrug compounds of the formula I-A; nanoparticles thereof; pharmaceutical compositions thereof; methods of treating, inhibiting, or preventing an HIV infection in a subject.

The first invention of Group I+ is restricted to a prodrug compound of the formula I-A and pharmaceutically acceptable salts thereof wherein ring A is (II-A), the stereochemistry of an asymmetric carbon represented by * has R- configuration; m is 0; R is (L)n-R1; L is absent; n is 0; R1 is H; nanoparticles thereof; pharmaceutical compositions thereof; methods of treating, inhibiting, or preventing an HIV infection in a subject. It is believed that claims 1 and 9-29 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. Each additional elected formula(e) requires the selection of a single definition for each compound variable. An exemplary election would be a prodrug compound of the formula I-A and pharmaceutically acceptable salts thereof wherein ring A is (II-B), the stereochemistry of an asymmetric carbon represented by * has R- configuration; m is 0; R is (L)n-R1; L is absent; n is 0; R1 is H; nanoparticles thereof; pharmaceutical compositions thereof; methods of treating, inhibiting, or preventing an HIV infection in a subject. 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 m, ring A, and R.

The Groups I+ share the technical features of a prodrug compound having the core structure of the formula I-A; a nanoparticle comprising the prodrug compound, and at least one surfactant; a pharmaceutical composition comprising at least one nanoparticle and at least one pharmaceutically acceptable carrier; a method for treating an HIV infection in a subject in need thereof, said method comprising administering to said subject a prodrug compound and a nanoparticle; a method for inhibiting an HIV infection in a subject in need thereof, said method comprising administering to said subject a prodrug compound and a nanoparticle; and a method for preventing an HIV infection in a subject in need thereof, said method comprising administering to said subject a prodrug compound and a nanoparticle. However, these shared technical features do not represent a contribution over the prior art.

Specifically, US 2014/0221378 A1 to Japan Tobacco Inc. teaches a prodrug compound having the core structure of the formula I-A (Para. [1868];...see compound 37...); a pharmaceutical composition (Claim 12) comprising at least one nanoparticle (Para. [0077], A pharmaceutical composition comprising a compound having an anti-HIV action and a pharmaceutically acceptable carrier, wherein the compound having an anti-HIV action is a compound of any one of the above-mentioned [1] to [11] or a pharmaceutically acceptable salt thereof alone.) and at least one pharmaceutically acceptable carrier (Claim 12; Para. [0077]); a method for treating an HIV infection (Para. [0077]), inhibiting an HIV infection (Para. [0077]), preventing an HIV infection in a subject in need thereof (Para. [0963]), said method comprising administering to said subject a prodrug compound (Claims 18-20).

Additionally, US 2013/0171214 A1 to ViiV Healthcare Company teaches a compound with proven antiviral activity (Para. [0010];...see shown structure...) a nanoparticle (Claims 1 and 9; Paras. [0084] through [0088], Example 2) comprising the prodrug compound, and at least one surfactant (Claim 1; Paras. [0013] and [0014]).

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