PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2015/055095	06.07.2015	08.07.2014

International Patent Classification (IPC) or both national classification and IPC
INV. C07D209/44 A61K31/4035 A61K31/454 C07D407/10 C07D401/06 C07D407/06 A61K31/4439 A61K31/4178 A61K31/5377 A61K31/55 A61K31/541 C07D417/06 C07D413/06 A61K31/496 A61K31/5386 C07D403/06

Applicant
VIIV HEALTHCARE UK LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Sarakinos, Georgios Telephone No. +49 89 2399-0

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2015/055095

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established 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).

4. ☐ 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.

5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-17
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-17
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The present application discloses isoindoline compounds for use in the treatment of infections caused by the HIV. The application also discloses processes for the synthesis of these compounds.

2. Reference is made to the following documents:

D1 WO 2014/009794 A1 (VIIV HEALTHCARE UK LTD [GB]) 16 January 2014 (2014-01-16)

D2 WO 2013/134142 A1 (SQUIBB BRISTOL MYERS CO [US]) 12 September 2013 (2013-09-12)

D3 WO 2013/103738 A1 (GILEAD SCIENCES INC [US]; BABAOGLU KERIM [US]; BRIZGYS GEDIMINAS [US];) 11 July 2013 (2013-07-11)

D4 WO 2013/012649 A1 (GLAXOSMITHKLINE LLC [US]; DE LA ROSA MARTHA ALICIA [US]; JOHNS BRIAN A) 24 January 2013 (2013-01-24)

D5 WO 2009/030316 A1 (MERCK PATENT GMBH [DE]; EGGENWEILER HANS-MICHAEL [DE]; SIRRENBERG CHRI) 12 March 2009 (2009-03-12)

D6 WO 2008/155001 A1 (MERCK PATENT GMBH [DE]; BUCHSTALLER HANS-PETER [DE]; EGGENWEILER HANS-) 24 December 2008 (2008-12-24)

3. Novelty [Art 33(2) PCT]

Documents D3, D5 and D6 disclose isoindoline compounds. One feature that renders the compounds of Formula I novel over the compounds and Markush formulas disclosed in documents D3, D5 and D6 is the appendage -$C(OR^1)CO_2H$. This group is not anticipated by the Markush formulas in documents D3, D5 and D6.

Documents D1, D2 and D4 disclose compounds whoso "core" fused bicyclic ring is a heterocycle other than isoindoline.

Hence, the compounds of formula I of claim 1 are novel and thus, claims 1-17 meet the requirements of Novelty [Art 33(2) PCT].

4. Inventive step [Art 33(3) PCT]

Document D1 may be considered to be the closest prior art to the present application as it discloses 1*H*-pyrrolo[2,3-*b*]pyridines as inhibitors of HIV replication in subjects infected with HIV. Starting from document D1, the objective technical problem to be solved by the present application may be viewed as the provision of further inhibitors of HIV replication. The applicant provides the compounds of formula I as a solution to the technical problem. There are several structural differences between the compounds of formula I in claim 1 of the present application (they are isoindolines) and the 1*H*-pyrrolo[2,3-*b*]pyridines of document D1. Therefore, starting from document D1, the isoindolines of formula I of the present application would not have been obvious as inhibitors of HIV replication to the person skilled in the art. Furthermore, the applicant provides in the description of the application IC50 data from an MT4 assay for 326 compounds that fall under the scope of formula I of claim 1. The data supports the claims. It can be assumed therefore that the objective technical problem has been solved in a non-obvious way. Hence, the compounds of formula I of claim 1 are inventive and thus, claims 1-17 meet the requirements of inventive step [Art 33(3) PCT].

5. Method of Treatment

Claims 13 and 14 relate to subject-matter considered by this Authority to be covered by the provision of Rule 39.1(iv) PCT. The patentability can be dependent upon the formulation of the claim. The EPO, for example, does not recognize as patentable claims to the use of a compound in medical treatment, but may allow claims to a product in particular substances or compositions for use in a first or further medical treatment.