

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.
PCT/EP2015/071776

International filing date (day/month/year)
22.09.2015

Priority date (day/month/year)
26.09.2014

International Patent Classification (IPC) or both national classification and IPC
INV. C07D471/04 A61P11/00 A61K31/4375

Applicant
GLAXOSMITHKLINE INTELLECTUAL PROPERTY...

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 notified 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:



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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

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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 43bis.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 13ter.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 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.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. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

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

1. Statement

Novelty (N)	Yes: Claims	<u>1-16</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-16</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-16</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Item V

Reference is made to the following documents:

- D1 WO 2005/082889 A1 (JANSSEN PHARMACEUTICA NV [BE]; DE CORTE BART [US]; KINNEY WILLIAM A [U] 9 September 2005 (2005-09-09)
- D2 WO 01/24797 A1 (MERCK & CO INC [US]; ASKEW BEN C [US]; SMITH GARRY R [US]) 12 April 2001 (2001-04-12)

The present application is directed alpha_vbeta₆ integrin antagonists which are useful for the treatment of e.g. fibrotic diseases. None of D1 or D2 discloses any of the claimed naphthyridine derivatives. The requirements of Art. 33(2) PCT are met.

The problem to be solved may be regarded the provision of alternative alpha_vbeta₆ integrin antagonists which are useful for the treatment of e.g. fibrotic diseases. Both D1 and D2 disclose naphthyridine derivatives. However, the specific substituent including a pyrrolidin-butanoic acid moiety is not suggested in these documents. The claimed subject-matter according to claims 1-16 may be regarded non-obvious. The description (pages 36-37) includes activity data for select compounds.

The requirements of Art. 33(3) PCT appear of having been met for claims 1-16.

Claims 1 shall include "pharmaceutically acceptable" salt (Art. 6 PCT).

Claims which include only the mechanism of action (claims 5, 9 and 16) are not acceptable since their scope is unclear (Art. 6 PCT).

Claims 8-13 relate to a subject-matter considered by this Authority to be covered by the provision of Rule 39.1(iv)/67.1(iv) PCT.

The patentability can be dependent upon the formulation of the claims. 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 in a first or further medical treatment.

Patentability, in particular novelty and inventive step, of claims 8-13 has been assessed on the basis of a purpose-limited product claim taking into account the alleged effects of the compounds.

Item VI

Reference is made to the following document:

D3 WO 2014/154725 A1 (GLAXOSMITHKLINE IP DEV LTD [GB]) 2 October
 2014 (2014-10-02)

This document does not reveal any specific compounds being embraced by the present application. No compound bearing a group $\text{-OCH}_2\text{-CH}_2\text{-O-CH}_3$ has been specified or suggested in this document.