

**PATENT COOPERATION TREATY**

**TRANSLATION**

From the  
INTERNATIONAL SEARCHING AUTHORITY

**PCT**

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing  
(day/month/year)

Applicant's or agent's file reference <b>091485</b>	<b>FOR FURTHER ACTION</b> See paragraph 2 below
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International application No. <b>PCT/JP2009/071811</b>	International filing date (day/month/year) <b>28.12.2009</b>	Priority date (day/month/year) <b>29.12.2008</b>
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International Patent Classification (IPC) or both national classification and IPC

Applicant  
**TAKEDA PHARMACEUTICAL COMPANY 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 43bis.1(a)(i) with regard to novelty, inventive step or 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 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 66.1bis(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.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Date of completion of this opinion	Authorized officer
Facsimile No.		Telephone No.

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Box No. I	Basis of this opinion
	<p>1. With regard to the <b>language</b>, this opinion has been established on the basis of:</p> <p><input checked="" type="checkbox"/> the international application in the language in which it was filed</p> <p><input type="checkbox"/> 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)).</p> <p>2. <input type="checkbox"/> This opinion has been established taking into account the <b>rectification of an obvious mistake</b> authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))</p> <p>3. With regard to any <b>nucleotide and/or amino acid sequence</b> disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:</p> <p>a. type of material</p> <p><input type="checkbox"/> a sequence listing</p> <p><input type="checkbox"/> table(s) related to the sequence listing</p> <p>b. format of material</p> <p><input type="checkbox"/> on paper</p> <p><input type="checkbox"/> in electronic form</p> <p>c. time of filing/furnishing</p> <p><input type="checkbox"/> contained in the international application as filed</p> <p><input type="checkbox"/> filed together with the international application in electronic form</p> <p><input type="checkbox"/> furnished subsequently to this Authority for the purposes of search</p> <p>4. <input type="checkbox"/> In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.</p> <p>5. Additional comments:</p>

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

the entire international application

claims Nos. 21

because:

the said international application, or the said claims Nos. 21 relate to the following subject matter which does not require an international search (*specify*):

Claim 21 pertains to methods for treatment of the human body by therapy.

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

no international search report has been established for said claims Nos. 21

a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).

a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

See Supplemental Box for further details.

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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)	Claims <u>1-20, 22</u>	YES
		Claims _____	NO
	Inventive step (IS)	Claims _____	YES
		Claims <u>1-20, 22</u>	NO
	Industrial applicability (IA)	Claims <u>1-20, 22</u>	YES
		Claims _____	NO
2. Citations and explanations:			
<p>Document 1: WO 2007/037534 A1 (Banyu Pharmaceutical Co., Ltd.), 05 April 2007</p> <p>Document 2: WO 2008/050821 A1 (Takeda Pharmaceutical Co. Ltd.), 02 May 2008</p> <p>Document 3: WO 2006/112549 A1 (Takeda Chemical Industries, Ltd.), 26 October 2006</p> <p>The invention as in claims 1-20 and 22 does not involve an inventive step in the light of documents 1, 2, and 3 cited in the ISR, as explained below.</p> <p>The claims and examples in document 1 cited in the ISR disclose various 2-heteroaryl substituted indole derivatives, and indicate that these derivatives have a glucokinase activating effect.</p> <p>The compound of the invention as in claims 1-20 and 22 differs, when compared with the abovementioned derivatives disclosed in document 1, in that the ring at the 2-position is stipulated to be a five- to seven-membered non-aromatic nitrogen-containing heterocycle.</p> <p>However, since the respective examples in documents 2 and 3 cited in the ISR indicate that a non-aromatic</p>			

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**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

nitrogen-containing heterocycle such as a thiazoline ring is used as a cyclic group in the 2-position of an indole derivative having glucokinase activity, a person skilled in the art could easily achieve the invention as in claims 1-20 and 22.

Moreover, even considering the examples in the description of the present application, it is not found that the characterizing features of the invention as set forth in claims 1-20 and 22 provide an especially notable effect.

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<b>Box No. VI</b>	<b>Certain documents cited</b>												
1. Certain published documents (Rule 43bis.1 and 70.10)													
<table style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: center; border-bottom: 1px solid black;">Application No. Patent No.</th> <th style="text-align: center; border-bottom: 1px solid black;">Publication date (day/month/year)</th> <th style="text-align: center; border-bottom: 1px solid black;">Filing date (day/month/year)</th> <th style="text-align: center; border-bottom: 1px solid black;">Priority date (valid claim) (day/month/year)</th> </tr> </thead> <tbody> <tr> <td style="padding: 5px;"><b>KR 2009-033752 A</b> <b>[E, X]</b></td> <td style="text-align: center; padding: 5px;">06.04.2009</td> <td style="text-align: center; padding: 5px;">01.10.2007</td> <td></td> </tr> <tr> <td style="padding: 5px;"><b>WO 2009/025477 A1</b> <b>[E, X]</b></td> <td style="text-align: center; padding: 5px;">26.02.2009</td> <td style="text-align: center; padding: 5px;">18.08.2008</td> <td style="text-align: center; padding: 5px;">17.08.2007</td> </tr> </tbody> </table>	Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)	<b>KR 2009-033752 A</b> <b>[E, X]</b>	06.04.2009	01.10.2007		<b>WO 2009/025477 A1</b> <b>[E, X]</b>	26.02.2009	18.08.2008	17.08.2007	
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2. Non-written disclosures (Rule 43bis.1 and 70.9)													
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**Box No. VIII**      **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

In claims 17-18 and 22, the expression "prodrug" used to explain the chemical structure of a compound is not clear, and the technical scope thereof cannot be understood or specified, even with reference to the description of the present application; therefore, it cannot be said that claims 17-18 and 22 are clear in the sense of PCT Article 6.

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**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

C07D417/14 (2006.01) i, A61K31/427 (2006.01) i,  
A61K31/4439 (2006.01) i, A61K31/5377 (2006.01) i,  
A61K31/541 (2006.01) i, A61P3/04 (2006.01) i,  
A61P3/10 (2006.01) i, A61P43/00 (2006.01) i