

Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 13-236627-00017-0000

Fecha: 2015-11-23 17:10:27 Dep. 2020 DIR NUEVASCF
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Act 412 REPOSPRESRECU Folios 12

REF:

Expediente No. PCT/13-236627

TÍTULO SOLICITADO: “COMPOSICIÓN FARMACÉUTICA QUE
COMPRENDE UNA COMBINACIÓN DE LOS
COMPUESTOS 2-AMINO-N-[7-METOXI-8-(3-
MORFOLIN-4-ILPROPOXI)-2, 3-
DIHIDROIMIDAZOL [1,2-C] QUINAZOLIN-5-
IL]PIRIMIDIN-5-CARBOXAMIDA Y 4-[4-[[2-(4-
CLOROFENIL) FENIL]METIL]PIPERAZIN-1-IL]-
N-[4-[[2-(2R)-4-(DIMETILAMINO)-1-
FENILSULFANILBUTAN-2-IL]AMINO]-3-
NITROFENIL]SULFONIL BENZAMIDA ÚTIL
PARA EL TRATAMIENTO DE CÁNCER DE
MAMA”

PUBLICACIÓN:

Gaceta 681 del 16/12/2013, N° de publicación 1852.

SOLICITANTE:

BAYER INTELLECTUAL PROPERTY GMBH.

APODERADO:

CARLOS REINALDO OLARTE GARCÍA.

TRÁMITE:

Recurso de Reposición y en subsidio el de apelación en
contra de la Resolución 79659 de septiembre 30 de
2015 por la cual se concede una patente de invención
tramitada bajo el número de expediente PCT/13-
236627.

TITO NOÉ PARRA MURILLO, mayor de edad, identificado como aparece al pie de
mi firma, reconocido apoderado de la sociedad LAFRANCOL S.A.S. en el asunto de
la referencia, de manera respetuosa, y dentro de los términos de ley, presento Recurso

de Reposición y en subsidio de apelación contra la Resolución 79659 de septiembre 30 de 2015 por la cual se concedió a la solicitud PCT/13-236627 el privilegio de patente de invención.

I. PETICIÓN

Sírvase, Señor Superintendente, reponer íntegramente la Resolución 79659 de septiembre 30 de 2015, por la cual se declaró infundada la oposición presentada y se otorgó el privilegio de patente solicitado en el expediente de la referencia, y en su remplazo emitir otra que, con fundamento en los argumentos expuestos en el escrito de observación y en el presente escrito, declare fundada dicha oposición y niegue el privilegio de patente mencionado, procediendo luego al definitivo archivo del expediente en cuestión.

II. ARGUMENTOS SOBRE LOS FUNDAMENTOS DE LA CONCESIÓN Y MOTIVOS DE INCONFORMIDAD

La Resolución 79659 de septiembre 30 de 2015, que concede el privilegio de patente de invención solicitado para el capítulo reivindicatorio del expediente 13-236627 del título de referencia, viola flagrantemente la Decisión 486 si se tiene en cuenta que existían motivos suficientes para afectar los requisitos de novedad y nivel inventivo de la solicitud en mención. Es evidente que el solicitante y la Resolución cometen un error cuando afirman que la oposición presentada por mi representada no muestra ningún tipo de argumento soportado técnicamente, ni desvirtúa la patentabilidad del objeto de estudio, declarándola infundada por cuanto, al momento de presentación del escrito de oposición se dejó en claro que para el presente caso nos encontramos frente a una combinación de compuestos, lo cual indudablemente afecta el requisito de nivel inventivo, éste mismo indispensable para acceder a cualquier beneficio patentario.

Así las cosas, me permito reiterar que la concesión de patente objeto del presente escrito se ve afectada por los documentos del estado del arte que fueron presentados inicialmente en el escrito de observación, por lo cual, basado en lo siguiente, solicito respetuosamente a ese Despacho dar análisis completo y a cabalidad sobre los siguientes documentos, los cuales sin lugar a dudas objetan la concesión en mención, toda vez que develan de manera expresa y sucinta lo que se pretende proteger en la

presente solicitud.

También es necesario reiterar que la solicitud de la referencia pretende proteger mediante el derecho patentario objetos que no son considerados invenciones. Es claro que una invención es toda creación humana que permita transformar la materia o energía que existe en la naturaleza, para su aprovechamiento por los seres humanos y satisfacer sus necesidades concretas. De igual modo, como ya se mencionó, según los parámetros de la Decisión 486 y normas concordantes, serán patentables las invenciones que cumplan con los requisitos de novedad, nivel inventivo y aplicación industrial. No obstante, puede observarse que la solicitud en comento pretende reivindicar combinaciones, las cuales no se consideran invenciones. En este sentido, la mezcla (Combinaciones) de productos (Moléculas) conocidos y su variación, bien sea en uso, forma, dimensión o de materia, NO se consideran invenciones por cuanto no son susceptibles de aplicación industrial, nivel inventivo y novedad, luego NO pueden acceder a beneficios patentarios. Por lo tanto, se suma una circunstancia más que imposibilita definitivamente la concesión de la solicitud en mención.

Y sobre el particular, es imprescindible señalar que un efecto sinérgico nuevo no se considera inventivo como tal, dado que puede ser obvio para una persona versada en la materia, cosa que sucede en el presente caso. En palabras del Doctor Carlos Correa, *“El efecto sinérgico entre dos o más drogas se puede considerar un “descubrimiento” y no una “invención”, dado que la sinergia ocurre en el cuerpo y se descubre a través de ensayos clínicos. Asimismo, cabe destacar que, en algunos casos, las reivindicaciones de combinaciones pueden equivaler, en términos prácticos, a reivindicaciones sobre tratamientos médicos (cuya patentabilidad está excluida en la mayoría de los países), cuando sólo brindan un método para administrar una combinación de drogas conocidas. Asimismo, la combinación de drogas para evitar la resistencia particular a una de ellas es una práctica normal en el desarrollo farmacéutico y, por lo general, es evidente para el hombre del oficio de nivel medio”* (Pautas para el examen de patentes farmacéuticas, CEIDIE, Pág. 8). En estos términos, está claro que nos encontramos frente a un tema totalmente sensible que merece toda la evaluación por cuanto las combinaciones deben considerarse excluidas de beneficios de patente.

Y en caso que ese Despacho decidiera insistir en el cabal cumplimiento de los requisitos exigidos para acceder al beneficio de patente, me permito allegar copia del International Search Report y el respectivo Written Opinion Of The International Searching

Authority, documentos en los cuales se resalta que la presente invención no cumple con los requisitos de novedad y nivel inventivo por cuanto existen documentos citados del estado del arte que afectan de manera definitiva tales exigencias. Lo anterior deja entrever, sin lugar a equívocos, que la presente solicitud no debió ser concedida, por lo cual es procedente la revocatoria de la Resolución objeto de este escrito.

En este sentido, reitero con el debido respeto la necesidad de analizar a profundidad los requisitos de novedad y nivel inventivo para así determinar si la presente solicitud es merecedora de concesión de privilegio de patente.

ANEXOS

International Search Report y el Written Opinion Of The International Searching Authority de la equivalente internacional WO 2012/136549

En subsidio apelo.

Señor Superintendente,



TITO NOÉ PARRA MURILLO

C.C. 79.579.680 de Bogotá

T.P. 71168 del C. S de la J.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference BHC113027 - WO	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2012/055595	International filing date (day/month/year) 29/03/2012	(Earliest) Priority Date (day/month/year) 05/04/2011
Applicant BAYER PHARMA AKTIENGESELLSCHAFT		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 10 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out 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)).

- b. ☐

This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

- c. ☐

With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒

Certain claims were found unsearchable (See Box No. II)

3. ☒

Unity of invention is lacking (see Box No. III)

4. With regard to the **title**,



the text is approved as submitted by the applicant



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant



the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____



as suggested by the applicant



as selected by this Authority, because the applicant failed to suggest a figure



as selected by this Authority, because this figure better characterizes the invention

- b. ☐

none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/055535

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 additional 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 an additional fee, 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.:
1-15
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.

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2012/055595

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K31/517 G01N33/48 A61P35/00
ADD.

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)

A61K G01N A61P

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)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TORBETT NEIL E ET AL: "A chemical screen in diverse breast cancer cell lines reveals genetic enhancers and suppressors of sensitivity to PI3K isoform-selective inhibition", BIOCHEMICAL JOURNAL, vol. 415, no. Part 1, October 2008 (2008-10), pages 97-110, XP002674479, figure 3	1-14
X,P	----- WO 2011/128407 A2 (BAYER PHARMA AG [DE]; LIU NINGSHU [DE]) 20 October 2011 (2011-10-20) claims 1,8,9 page 65, lines 13,14,32 ----- -/--	1-13

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* 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

Z document member of the same patent family

Date of the actual completion of the international search

28 June 2012

Date of mailing of the international search report

05/07/2012

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Albayrak, Timur

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2012/055595

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation* of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WC 2008/070150 A1 (BAYER PHARMACEUTICALS CCRP [US]; HENTEMANN MARTIN [US]; WOOD JILL [US]) 12 June 2008 (2008-06-12) cited in the application page 40 claim 43	1-13
X	WO 2004/005481 A2 (UNIV COLUMBIA [US]; FISHER PAUL B [US]; SARKAR DEVANAND [US]; GOFALKRI) 15 January 2004 (2004-01-15) claim 72	15
X	WO 02/069896 A2 (NORTHWEST BIOTHERAPEUTICS INC [US]; HUANG RUO-PAN [US]; BOYNTON ALTON) 12 September 2002 (2002-09-12) claim 27	15
X	WO 2009/126172 A1 (UNIV COLUMBIA [US]; JOE ANDREW K [US]; WEINSTEIN I BERNARD [US]) 15 October 2009 (2009-10-15) claims 1-5	15
X	US 2009/275340 A1 (REED JOHN C [US] ET AL) 5 November 2009 (2009-11-05) claims 1-18	15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2012/055595

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011123407	A2	20-10-2011	NONE
WO 2008070150	A1	12-06-2008	AR 064106 A1 11-03-2009
		AU 2007328008 A1 12-06-2008	
		CA 2671614 A1 12-06-2008	
		CL 35082007 A1 04-07-2008	
		CN 101631464 A 20-01-2010	
		CO 6220908 A2 19-11-2010	
		CR 10838 A 05-11-2009	
		CU 20090103 A7 28-12-2011	
		DO P2009000135 A 30-06-2009	
		EA 200900733 A1 30-12-2009	
		EC SP099387 A 30-11-2009	
		EP 2096919 A1 09-09-2009	
		JP 2010511718 A 15-04-2010	
		KR 20090096440 A 10-09-2009	
		MA 31283 B1 01-04-2010	
		NZ 577342 A 12-01-2012	
		PA 8759601 A1 09-02-2009	
		PE 14442008 A1 29-11-2008	
		SG 177170 A1 30-01-2012	
		SV 2009003288 A 02-10-2009	
		TW 200840582 A 16-10-2008	
		US 2011083984 A1 14-04-2011	
		UY 30761 A1 03-07-2008	
		WC 2008070150 A1 12-06-2008	
		ZA 200904691 A 29-09-2010	
WO 2004005481	A2	15-01-2004	AU 2003256453 A1 23-01-2004
		CA 2491637 A1 15-01-2004	
		EP 1534073 A2 01-06-2005	
		JP 2005532070 A 27-10-2005	
		US 2005250127 A1 10-11-2005	
		WO 2004005481 A2 15-01-2004	
WO 02069896	A2	12-09-2002	AU 2002252160 A1 19-09-2002
		US 2004180846 A1 16-09-2004	
		US 2008138337 A1 12-06-2008	
		US 2012045501 A1 23-02-2012	
		WO 02069896 A2 12-09-2002	
WO 2009126172	A1	15-10-2009	NONE
US 2009275040	A1	05-11-2009	US 2009275040 A1 05-11-2009
			US 2012046195 A1 23-02-2012

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-14

Use of 2,3-dihydroimidazo[1,2-c]quinazoline compounds of formula (I) for treating breast cancer. Compositions of 2,3-dihydroimidazo[1,2-c]quinazoline compounds and further agents as well as uses of biomarkers for predicting sensitivity and/or resistance of a patient with cancer to a 2,3-dihydroimidazo[1,2-c]quinazoline compound.

2. claim: 15(partially)

A method of determining the level of a component of Bcl expression.

3. claim: 15(partially)

A method of determining the level of a component of HER family expression.

4. claim: 15(partially)

A method of determining the level of a component of one or more of PIK3CA signaling.

5. claim: 15(partially)

A method of determining the level of a component of one or more of loss of PTEN.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.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/EP2012/055595	International filing date (day/month/year) 29.03.2012	Priority date (day/month/year) 05.04.2011
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International Patent Classification (IPC) or both national classification and IPC
INV. A61K31/517 G01N33/48 A61P35/00

Applicant
BAYER PHARMA AKTIENGESELLSCHAFT

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 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 66.1bis(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:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0
Fax: +49 89 2399 - 4465

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Albayrak, Timur

Telephone No. +49 89 2399-0



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2012/053595

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 filed or furnished:
 - a. (means)
 - ☐ on paper
 - ☐ in electronic form
 - b. (time)
 - ☐ in the international application as filed
 - ☐ together with the international application in electronic form
 - ☐ subsequently to this Authority for the purposes of search
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 in 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:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2012/055595

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. 15

because:

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

☐ 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 the whole application or for said claims Nos. 15

☐ 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 Rules 13ter.1(a) or (b).

☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2012/055595

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☒ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-15

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	
	No: Claims	<u>1-15</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-15</u>
Industrial applicability (IA)	Yes: Claims	<u>1-15</u>
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2012/055595

Box No. VI Certain documents cited

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

and / or

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

see form 210

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:

see separate sheet

Claim 15 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 39.1(iv) / 67.1(v) PCT.

The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise 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.

Re Item IV

The present application has been found to include the following two inventions:

(1) Claims 1-14 relate to subject-matter described by the following features:

Use of 2,3-dihydroimidazo[1,2-c]quinazoline compounds of formula (I) for treating breast cancer. Compositions of 2,3-dihydroimidazo[1,2-c]quinazoline compounds and further agents as well as uses of biomarkers for predicting sensitivity and/or resistance of a patient with cancer to a 2,3-dihydroimidazo[1,2-c]quinazoline compound.

(2) Claim 15 is directed to a method of determining the level of a component of one or more of Bcl expression, HER family expression and/or activation, PIK3CA signaling and/or loss of PTEN.

Since the claims do not have any same technical features, they cannot be described as being linked by same special technical features (STF).

The problems solved by the above mentioned groups of features (1) and (2) are:

(i) firstly the problem of treating or preventing breast cancer (see also claims 1-14 and pages 11-15),

(ii) secondly the problem of determining the level of a component of one or more of Bcl expression, HER family expression and/or activation, PIK3CA signaling and/or loss of PTEN (see also claim 15 and page 15).

Since the problems solved / technical effects of the two groups of claims are different, they cannot be described as being linked by corresponding STF.

It follows that claims 1-14 and claim 15 are not linked by same or corresponding STF so that they form a novel and inventive general linking concept.

Thus, the present application comprises *a priori* two distinct inventions characterized by the technical features as indicated above (items (1) and (2)).

Moreover, the subject-matter of claim 15 is described to solve the problem of determining the level of a component of one or more of Bcl expression, HER family expression and/or activation, PI3CA signaling and/or loss of PTEN (page 15 lines 21-24).

The technical features solving the problem, as described by the present description and reflected by the present claims is a method of determining the level of a component of one or more of Bcl expression, HER family expression and/or activation, PIK3CA signaling and/or loss of PTEN, wherein in said Bcl expression, said component is Bcl, for example, wherein in said HER family expression and/or activation, PIK3CA signaling, said component is EGF-R for example, and wherein said loss of PTEN, said component is PTEN, for example (see also claim 15).

Thus, the single general inventive concept linking the different alternatives in claim 15 and solving the problem posed is the provision of a method of determining the level of a component of one or more of Bcl expression, HER family expression and/or activation, PIK3CA signaling and/or loss of PTEN.

However, this concept is already known from WO2004005481, WO02069896, WO2009126172 and US20090275040. All of these documents disclose methods of determining expression of Bcl (see the passages cited in the search report).

These documents, therefore anticipate the single general inventive concept linking the different subjects contained in claim 15.

Therefore, this concept can no longer serve as single general inventive concept in the sense of Rule 13(1) PCT, linking the different subjects together.

Since there is no other concept that could fulfil the role of single general inventive concept in the sense of Rule 13(1) PCT, present claim 15 lacks unity of invention *a posteriori*.

As explained above, the application lacks unity of invention and the inventions have been grouped as indicated in the search report. As for the subjects of claim 15, only the first invention has been searched. No further invitation to pay further additional fees will be issued. This is because Article 17(3)(a) PCT stipulates that the ISA shall establish the International Search Report on those parts of the international application which relate to the invention first mentioned in the claims ('main invention') and for those parts which relate to inventions in respect of which the additional fees were paid. Neither the PCT nor the PCT guidelines provide a legal basis for further invitations to pay further additional search fees (W17/00, point 11 and W1/97, points 11-16). The non-searched subject-matters may be the subject of one or more divisional applications (see W18/07, point 26).

Note: as searching the remaining subjects would have caused major additional searching effort, only the subjects of claims 1-14 and a method of determining the level of a component of Bcl expression, has been searched but not the other subjects contained in claim 15. Claim 15, thus, has been searched only in part.

Note: Although some of the cited documents might also be pertinent for the other inventions this does not imply that a full search has been carried out for these inventions.

Re Item V

Reference is made to the following documents; unless otherwise indicated, reference is made to the relevant passages emphasized in the Search Report.

- D1 TORBETT NEIL E ET AL: "A chemical screen in diverse breast cancer cell lines reveals genetic enhancers and suppressors of sensitivity to P 3K isoform-selective inhibition";
BIOCHEMICAL JOURNAL,
vol. 415, no. Part 1, October 2008 (2008-10), pages 97-110,
XP002674479,
- D2 WO 2011/123407 A2 (BAYER PHARMA AG [DE]; LIU NINGSHU [DE]) 20 October 2011 (2011-10-20)
- D3 WO 2008/070150 A1 (BAYER PHARMACEUTICALS CORP [US]; HENTEMANN MARTIN [US]; WOOD JILL [US]) 12 June 2008 (2008-06-12) cited in the application
- D4 WO 2004/005481 A2 (UNIV COLUMBIA [US]; FISHER PAUL B [US]; SARKAR DEVANAND [US]; GOPALKRI) 15 January 2004 (2004-01-15)
- D5 WO 02/069896 A2 (NORTHWEST BIOTHERAPEUTICS INC [US]; HUANG RUO-PAN [US]; BOYNTON ALTON) 12 September 2002 (2002-09-12)
- D6 WO 2009/126172 A1 (UNIV COLUMBIA [US]; JOE ANDREW K [US]; WEINSTEIN I BERNARD [US]) 15 October 2009 (2009-10-15)
- D7 US 2009/275040 A1 (FEED JOHN C [US] ET AL) 5 November 2009 (2009-11-05)

1 Art. 33(2) PCT)

- 1.1 D1 discloses the use of biomarkers to predict sensitivity and/or resistance of a patient with cancer to a compound according to claim 1. Thus, claim 14 lacks novelty.

- 1.2 D3 discloses combinations of compounds according to claims 1-7 and ABI-007, CCI-779, thymosin, gemcitabine, rapamycin or alpha glucosidase inhibitors for treating breast cancer.
Thus, claims 1-13 lack novelty.
- 1.3 D4-D8 disclose methods of determining expression of Bcl-2 or Bcl-B. Claim 15 therefore lacks novelty.
- 1.4 Art. 33(3) PCT
- 1.4.1 Claims 1-14 are not novel and do not involve an inventive step.
- 1.5 Notwithstanding the previous objections, claim 14 is not inventive as from D1 and D3 it is known that PIK3CA is involved in breast cancer development and that compounds of formula (I) are inhibitors of PIK3CA.

Re Item VI

Document D2 is cited under Rules 64.3 and 70.10 PCT.

Re Item VIII

The term "rapamycin analogue" is ambiguous