



No. 08-052309- -00002-0000

Fecha: 2008-08-19 16:24:43 Dep. 2020 NUECREACIONE
Tra. 11 PATENTEIYI Eva: 378 FASENACIONALI
Act. 444 RESPUESTAREQUE Folios: 21

CALLE 72 N° 5-83 5°. PISO

www.lloredacamacho.com

jllcco@lloredacamacho.com

Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

E. _____ S. _____ D. _____

Re: **P1.-ASTRAZENECA AB y ASTEX THERAPEUTICS LTD.-Solicitud de Patente de Invención en Fase Nacional PCT para "COMPUESTOS 2-AMINO-IMIDAZOL-4-ONA NOVEDOSOS Y SU USO EN LA FABRICACIÓN DE UN MEDICAMENTO PARA SER USADO EN EL TRATAMIENTO DEL DETERIORO COGNITIVO, LA ENFERMEDAD DE ALZHEIMER, NEURODEGENERACIÓN Y DEMENCIA".-Clase A61K 31/4178.-Expediente número 08-052.309.-**

1. Me refiero al auto dictado por ese Despacho notificado por fijación en lista el 27 de Junio de 2008.

2. Dando respuesta al mencionado auto me permito presentar a ese Despacho fotocopia debidamente autenticada del documento de representación legal que acredita a la suscrita ALICIA LLOREDADA y/o al doctor GUSTAVO TAMAYO, y/o a la doctor IGNACIO SANTAMARIA y/o a al doctor ENRIQUE ALVAREZ, en los términos del Párrafo 1º del Artículo 543 del Decreto-Ley 410 de 1971, como Representantes Legales en Bogotá para todos los asuntos relacionados con la Propiedad Industrial de la sociedad **ASTEX THERAPEUTICS LTD**, una sociedad organizada y existente de conformidad con las Leyes de Inglaterra y domiciliada en Cambridge. Reino Unido.

En consecuencia, atentamente solicito a ese Despacho reconocerme personería, en este asunto, de conformidad con el documento de Representación Legal para todos los asuntos de la Propiedad Industrial en Bogotá de **ASTEX THERAPEUTICS LTD** otorgado a favor de la SUSCRITA (ALICIA LLOREDADA) y/o al doctor GUSTAVO TAMAYO y/o al doctor IGNACIO SANTAMARIA y/o al doctor ENRIQUE ALVAREZ, de acuerdo con la copia debidamente autenticada ante Notario

Público que adjunto al presente expediente (Artículos 26 y 39 de la Decisión 486 de la Comunidad Andina de Naciones).

3. Con el texto del documento mencionado presento fotocopias, debidamente autenticadas por el Notario Sexto del Circulo de Bogotá, de:

- (a) Certificado Notarial expedido el 13 de Mayo de 2008 que acredita la existencia y representación del solicitante, debidamente apostillado;
- (b) Copia auténtica de la Traducción Oficial No. 2008-06-10-408, correspondiente a las partes pertinentes del documento anterior, también debidamente legalizada hasta por el Ministerio de Relaciones Exteriores bajo el número 775256 de 12 de Junio de 2008.

4. Cabe resaltar que el documento de Representación Legal que acredita a la suscrita ALICIA LLOREDA y/o al doctor GUSTAVO TAMAYO, y/o a la doctor IGNACIO SANTAMARIA y/o a al doctor ENRIQUE ALVAREZ, en los términos del Párrafo 1º del Artículo 543 del Decreto-Ley 410 de 1971, como Representantes Legales en Bogotá para todos los asuntos relacionados con la Propiedad Industrial de la sociedad **ASTRAZENECA AB**, organizada y existente de conformidad con las Leyes de Suecia y domiciliada en Södertälje, Suecia, fue presentado junto con la solicitud de patente de la referencia.

5. Así mismo, anexo me permito presentar a usted documento completo de la Opinión Escrita de la Autoridad de Búsqueda Internacional, correspondiente a la solicitud internacional número PCT/SE2006/001317, actualmente en trámite de Fase Nacional en ese despacho, bajo el número de la referencia.

6. Ruego a usted tomar atenta nota de lo anterior y proceder de conformidad.

Señor Superintendente,


ALICIA LLOREDA RICAURTE

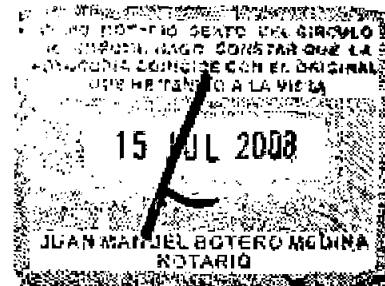
T.P.53.215

Poder de Representación Legal, documento escrito en inglés y en español.

(firma: ilegible)

Notario Público en y para Cambridge, Inglaterra

Mi comisión es de por vida.



APOSTILLA

(Convención de La Haya del 5 de Octubre de 1961)

Reino Unido de la Gran Bretaña e Irlanda del Norte

1. País: Reino Unido de la Gran Bretaña e Irlanda del Norte
Este documento público
2. ha sido firmado Peter Coleman Fletcher
3. actuando como Notario Público
4. lleva el sello/estampilla de dicho Notario Publico

CERTIFICADO

5. en Londres
6. el 19 de mayo de 2008
7. por el Secretario de Estado Principal de Su Majestad para Asuntos Exteriores y del Commonwealth
8. Número: H782297
9. Sello/Estampilla:
Sello de la Oficina de Asuntos Exteriores y del Commonwealth
10. Firma: (ilegible)
R. Bawden
Por el Secretario de Estado.

Si este documento se va a usar en un país que no es parte de la Convención de La Haya del 5 de octubre de 1961, debe presentarse a la sección consular de la misión que representa a ese país. Una apostilla o certificado de legalización únicamente confirma que la firma, sello o estampilla sobre el documento es autentica. No significa que los contenidos del documento sean correctos o que la Oficina de Asuntos Exteriores y del Commonwealth apruebe los contenidos.

Traducido según mi mejor saber y entender, este día 10 de junio de 2008 en la ciudad de Bogotá, D.C., por Anita Escobar de Tamayo, Traductora Oficial. Res. 2177 de 1989, Ministerio de Justicia, República de Colombia.

TRADUCTORA OFICIAL
RES. 2177 DE 1989 MINISTERIO DE JUSTICIA
ANITA ESCOBAR DE TAMAYO

Los abajo firmados,

Astex Therapeutics Ltd

con domicilio en

436 Cambridge Science Park
Milton Road, Cambridge
CB4 0QA, U.K.

nombramos por el presente a ALICIA LLOREDA y/o GUSTAVO TAMAYO y/o IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ, domiciliados en Bogotá, Colombia, con oficinas en dicha ciudad, Calle 72 No. 5-83, piso 6o., nuestros representantes legales y verdaderos en Bogotá, con facultades para recibir notificaciones y nombrar apoderados judiciales o extrajudiciales, con el fin de dar cumplimiento al parágrafo 1o. del artículo 543 del decreto 410 de 1971;

Los doctores ALICIA LLOREDA y/o GUSTAVO TAMAYO y/o IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ, o los apoderados que cualquiera de ellos designe, quedan especialmente facultados para representarnos ante las autoridades colombianas, administrativas, judiciales o de policía, en todos los trámites relativos a la propiedad industrial, a cuyo efecto les facultamos para dar ante dichas autoridades todos los pasos necesarios al objeto indicado; elevar solicitudes, declaraciones, reclamos, recursos y presentar desistimientos; formular descripciones, enmiendas, limitar el alcance de las solicitudes, presentar oposiciones y apelaciones; instaurar cancelaciones, renunciar total o parcialmente a los registros, abonar todos los impuestos y cuotas y efectuar todo otro pago determinado por la ley; recibir todos los documentos y valores, dando el descargo respectivo; llenar cualesquiera otros requisitos y tomar, en fin, todas las medidas que creyeren conducentes al resguardo de nuestros intereses; y en caso de producirse oposición, pasando los antecedentes a los tribunales, quedan facultados para tomar intervención como demandantes o demandados ante los jueces que sean competentes, pudiendo transar, someter a árbitros, desistir, percibir y apelar, con todas las demás facultades que resulten necesarias, y por el presente declaramos desde ahora válido y bueno cuanto dichos representantes y/o los apoderados que cualquiera de ellos nombre hicieren en nuestro beneficio.

Asimismo, facultamos a los doctores ALICIA LLOREDA y/o GUSTAVO TAMAYO y/o IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ, para solicitar en la Oficina de Propiedad Industrial la protocolización de este documento y de cualquier poder que cualquiera de ellos otorgue a nombre nuestro.

Dado y firmado

The undersigned,

Astex Therapeutics Ltd.

domiciled at

436 Cambridge Science Park
Milton Road, Cambridge,
CB4 0QA, U.K.

hereby appoint, ALICIA LLOREDA and/or GUSTAVO TAMAYO and/or IGNACIO SANTAMARIA and/or ENRIQUE ALVAREZ, of Bogotá, Colombia, with offices in said town, Calle 72 No. 5-83, Sixth Floor, our true and legal representatives in Bogotá, with power to receive notifications and to appoint judicial or extrajudicial agents, so as to comply with paragraph 1o. of article 543 of decree 410 of 1971.

Doctors ALICIA LLOREDA and/or GUSTAVO TAMAYO and/or IGNACIO SANTAMARIA and/or ENRIQUE ALVAREZ, or the agents by any one of them appointed, are especially empowered to represent us before the administrative, judicial or police authorities of Colombia, in all proceedings pertaining to industrial property, for which purpose we authorize them to take before the said authorities all the necessary steps for the said end; to file petitions, declarations, claims, recourses and withdrawals; to draw up specifications; to file amendments; to limit the scope of applications, file oppositions; file cancellations total or partially waive registrations, to pay all installments and effect all other payments prescribed by law; to receive proper receipts, to comply with all other requirements and, in short, to take all those measures which they may deem fit for the protection of our interests; and in case of opposition, where the proceedings be passed over to the courts, we authorize said agents to act on our behalf, as complainants as well as defendants, before the competent judges, with full powers to make arrangements, to submit to arbitration, to collect, to appeal and, in short, with all the powers as may be required, and we hereby declare from now on as valid and good all that said representatives and/or the agents by any one of them appointed may do for our benefit.

We also authorize doctors ALICIA LLOREDA and/or GUSTAVO TAMAYO and/or IGNACIO SANTAMARIA and/or ENRIQUE ALVAREZ, to apply for protocolization of this document and of any power of attorney by any one of them conferred in our name, before the Office of Industrial Property.

Given and signed this 13th day of May 2008

NOTARY SHOULD EXECUTE OTHER SIDE

Harren Jhoti, CEO

RF

CERTIFICADO NOTARIAL (SOCIEDAD)

Reino Unido
Ciudad Cambridge

Hoy 13 de Mayo de 2008 compareció
Dr. Harren Jhoti a quien conozco y
de quien me consta que firmó el anterior documento,
y quien debidamente juramentado declaró y dijo que
éste es Presidente
de Astex Therapeutics
Ltd la compañía nombrada en
el documento que antecede, una sociedad
debidamente organizada y existente conforme a las
leyes de Inglaterra
domiciliada en la ciudad de Cambridge

legalmente constituida para un
periodo de duración que aún no ha terminado, que
ejerce su objeto social, conforme a las leyes de
Inglaterra

que el declarante está autorizado por dicha
Compañía para conferir este poder; que el sello
estampado por él al pie de tal poder, en nombre y en
representación de la expresada Compañía, es el
sello oficial de ella; y que el objeto para el cual se
confiere este instrumento está comprendido dentro
del de la sociedad.

El suscrito Notario ha visto los Estatutos de
incorporación firmados en Cardiff
U.K. con fecha 8 Marzo de 2006.

y certifica que de conformidad con la legislación de
dicho Estado la anterior declaración juramentada es
prueba suficiente de que los hechos sobre los que ella
versa son ciertos o verdaderos, de lo cual da fe.

Notary Public (Notario Público)

P. Fletcher

PETER COLEMAN FLETCHER

Notary Public and for

Cambridge Cycles

In Commission expires 01 Sept 2008

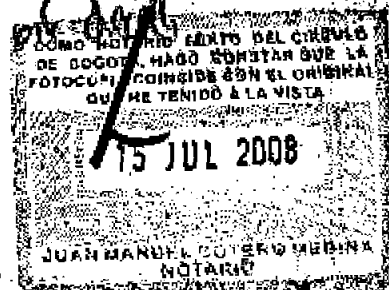
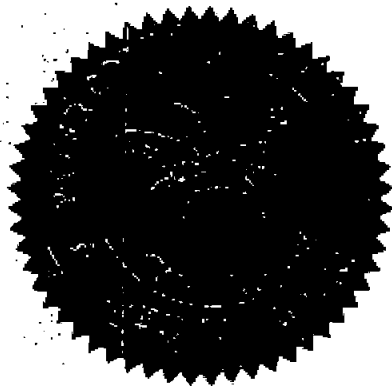
NOTARIAL CERTIFICATE (CORPORATION)

United Kingdom
City of Cambridge

On this 13th day of May 2008
personally
came Dr. Harren Jhoti
to me known, and known to me to be the person who
signed the foregoing instrument, who being by me
duly sworn did depose and say that he is the Chief
Executive Officer of Astex Thera-
peutics Ltd, the company named
within, a Corporation organized and existing under
the laws of England
domiciled at the City of Cambridge
legally constituted for a period of tenures not yet
expired, which exercises its corporate purposes
according to the laws of England
that the deponent is authorized by said Company to
confer this power of attorney; that the seal affixed
hereunto by the deponent in the name and on behalf
of said Corporation is the corporate seal thereof, and
that the purpose for which this instrument is granted
is included within the corporate purposes of the
Company.

The undersigned Notary Public has seen the articles
of Incorporation of said Corporation executed at

Cardiff U.K. under date of
8th March 2006 and hereby
certifies that under the laws of said State the
foregoing acknowledgment is sufficient proof that the
facts therein contained are true, which he attests.



APOSTILLE

(Hague Convention of 5 October 1961 / Convention de La Haye du 5 octobre 1961)

UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND

1. Country: United Kingdom of Great Britain and Northern Ireland
Pays: Royaume-Uni de Grande-Bretagne et d'Irlande du Nord

This public document / Le présent acte public

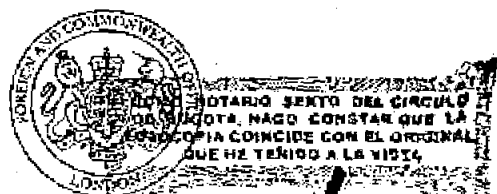
2. Has been signed by **Peter C Fletcher**
a été signé par
3. Acting in the capacity of **Notary Public**
agissant en qualité de
4. Bears the seal/stamp of **The Said Notary Public**
est revêtu du sceau/timbre de

Certified/Attesté

5. at London/à Londres
6. the/le 19 May 2008
7. by Her Majesty's Principal Secretary of State for Foreign and Commonwealth Affairs /
par le Secrétaire d'Etat Principal de Sa Majesté aux Affaires Etrangères et du Commonwealth.

8. Number/sous No **H782297**

9. Stamp:
timbre:
10. Signature: **R. Bawden**



15 JUL 2008

For the Secretary of State / Pour le Secrétaire d'Etat

If this document is to be used in a country which is not party to the Hague Convention of 5 October 1961, it should be presented to the consular section of the mission representing that country. An apostille or legalisation can only confirm that the signature, seal or stamp on the document is genuine. It does not mean that the contents of the document are correct or that the Foreign & Commonwealth Office approves of the contents.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
AstraZeneca
Global Intellectual Property
151 85 Södertälje
Sverige

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year) 27 -04- 2007

Applicant's or agent's file reference
102065-1 WO

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/SE2006/001317

International filing date (day/month/year)
20-11-2006

Priority date (day/month/year)
21-11-2005

International Patent Classification (IPC) or both national classification and IPC
See Supplemental Box

Applicant
AstraZeneca AB et al

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 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 opinions, see Form PCT/ISA/220.

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

Name and mailing address of the ISA/SE
Patent- och registreringsverket
Box 5055
S-102 42 STOCKHOLM

Facsimile No. +46 8 667 72 88

Authorized officer

Helena Melander/ELY

Telephone No. +46 8 782 25 00

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2006/001317

Supplemental Box

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

Continuation of: Cover sheet

International patent classification (IPC)

C07D 233/88 (2006.01)
A61K 31/4168 (2006.01)
A61K 31/4174 (2006.01)
A61K 31/4178 (2006.01)
A61K 31/427 (2006.01)
A61K 31/4439 (2006.01)
A61K 31/4725 (2006.01)
A61K 31/497 (2006.01)
A61K 31/506 (2006.01)
A61K 31/538 (2006.01)
A61P 25/16 (2006.01)
A61P 25/28 (2006.01)
C07D 233/86 (2006.01)
C07D 401/04 (2006.01)
C07D 401/10 (2006.01)
C07D 403/10 (2006.01)
C07D 405/04 (2006.01)
C07D 405/10 (2006.01)
C07D 405/14 (2006.01)
C07D 409/10 (2006.01)
C07D 413/10 (2006.01)
C07D 417/04 (2006.01)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2006/001317

Box No. I Basis of this 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. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material
☐ on paper
☐ in electronic form
 - c. time of filing/furnishing
☐ contained in the international application as filed.
☐ filed together with the international application in electronic form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table 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.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/SE2006/001317

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/SE2006/001317

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

The question 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. 1-28, 31-33, 36-42

because:

- ☒ the said international application, or the said claims Nos. 31-33, 36-42
relate to the following subject matter which does not require an international search (*specify*):

See PCT Rule 67.1.(iv): Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-28
are so unclear that no meaningful opinion could be formed (*specify*):

The general formula I with all the possibilities in variation of the groups R1, R2 and R3 generate so many answers that a meaningful search over the whole of the

.../...

- ☐ 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. _____
- ☐ 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 the Annex C-bis of the Administrative Instructions.
- ☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2006/001317

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: BOX III.2

claimed scope is impossible.

Furthermore, present claims 1-28 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and / or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts related to the compounds mentioned in claim 29 and compounds substituted with a phenyl (optionally further substituted) and another aryl or heteroaryl (optionally substituted) in position 5 of the 2-amino-imidazole-4-one.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2006/001317

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:

The following separate inventions were identified:

1: Claims 1-42 and partly claims 43-44 directed to the intermediate compounds of imidazole and thioxoimidazolidin (compare examples 3, 15-16, 19, 28-29, 36, 43-44, 46, 53, 68, 73, 78, 90-91, 95-96, 100-102, 105-106, 110-111, 117-118, 121, 123, 183-184, 186, 262, 264, 266, 276, 278-279, 286, 293, 298, 302, 332, 338, 342, 348 and 384-385 in the description).

2: Partly claims 43-44 directed to the intermediate compounds of 2-acetyl-1,2,3,4-tetrahydroquinoline and 2-acetyl-isoindoline (compare examples 1, 60 and 334 in the description).

3: Partly claims 43-44 directed to the intermediate compounds of 4,4,5,5-tetramethyl-1,3,2-dioxaborolan (compare examples 2, 7, 10, 24, 48, 61, 80, 82, 84, 114, 170 and 214 in the description).

.../...

4. Consequently, this opinion has been established in respect of the following parts of the international application:

☐ all parts

☒ the parts relating to claims Nos. Claims 1-42 and partly claims 43-44

Supplemental Box

In case the space in any of the preceding boxes is not sufficient,
Continuation of Box IV

4: Partly claims 43-44 directed to the intermediate compounds of [tert-butyl(diphenyl)silyloxy (compare examples 13-14, 33-35, 41-42, 86-89, 93-94, 98-99, 103-104, 108-109 and 380-383 in the description).

5: Partly claims 43-44 directed to the intermediate compounds of 1,2-diphenylethane-1,2-dione (compare examples 27, 52, 67, 72, 77, 116, 182, 261, 263, 265, 285, 292, 297, 301, 331, 337, 341 and 347 in the description).

6: Partly claims 43-44 directed to the intermediate compounds of 1,3-dithian (compare examples 40, 51, 66 and 330 in the description).

7: Partly claims 43-44 directed to the intermediate compounds of 1,1'-ethyne-1,2-diylidibenzene (compare examples 71, 76, 115, 181, 259-260, 284, 291, 296, 300, 336, 340 and 346 in the description).

8: Partly claims 43-44 directed to the intermediate compound of 3'-hydroxy-5'-methoxybiphenyl-3-carbaldehyd (compare example 85 in the description).

9: Partly claims 43-44 directed to the intermediate compound of 4-bromo-1-fluoro-2-methoxybenzene (compare example 113 in the description).

10: Partly claims 43-44 directed to the intermediate compound of 1-ethynyl-3-(3-methoxyphenoxy)benzene (compare example 258 in the description).

11: Partly claims 43-44 directed to the intermediate compound of 3-methoxypropan-1-sulfonyl chloride (compare example 268 in the description).

12: Partly claims 43-44 directed to the intermediate compound of 6-iodo-1,2,3,4-tetrahydronaphtalene (compare examples 70 and 283 in the description).

.../...

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2006/001317

Supplemental Box

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

13: Partly claims 43-44 directed to the intermediate compounds of 1-acetyl-5-iodoindoline and 1-acetyl-6-iodo-1,2,3,4-tetrahydroquinoline (compare examples 75 and 295 in the description).

14: Partly claims 43-44 directed to the intermediate compounds of 1,2,3,4-tetrahydronaphtalene-2-yl methyl ether (compare examples 288-290 in the description).

15: Partly claims 43-44 directed to the intermediate compounds of isochromene (compare examples 344-345 in the description).

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/SE2006/001317

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	* see below	YES
	Claims	* see below	NO
Inventive step (IS)	Claims	44**	YES
	Claims	1-30, 34-35, 43**	NO
Industrial applicability (IA)	Claims	1-30, 34-35, 43**-44**	YES
	Claims		NO

2. Citations and explanations:

*

Novelty

Claims 7, 11-14, 16, 19, 21, 24-29, 44** YES
Claims 1-6, 8-10, 15, 17-18, 20, 22-23, 30, 34-35, 43** NO

**

The opinion for claims 43-44 is only based on invention 1, see box IV.

The present invention relates to 2-amino-imidazole-4-one compounds and their use in the manufacture of a medicament to be used in the treatment of diseases such as cognitive impairment, Alzheimer's disease, neurodegeneration and dementia. The invention also comprises intermediate compounds.

Reference is made to the following documents:

D1: WO2005058311 A1
D2: Hydantoins, thiohydantoins, glycocyanidines. 36. 1,5,5- and 3,5,5-triphenyl derivatives. Simig, Gyula et.al. Tetrahedron (1973), 29(22), 3571-8.
D3: Synthesis and pharmacological action of Tetralin derivatives. III. Fujimura, Hajime et.al. Yakugaku Zasshi (1956), 76, 1151-3.
D4: US2005282825 A1
D5: US2006111370 A1
D6: WO2007005366 A1
D7: WO2007005404 A1

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: BOX V

Document D1 describes 2-amino-3,5-dihydro-5-[3-(1H-indol-5-yl)phenyl]-3-methyl-5-phenyl-4H-imidazole-4-one (RN:856885-25-1) and structurally related compounds. The compounds are used to treat neurodegenerative and cognitive diseases such as Alzheimer's. The compounds are also used in the combination with an effective amount of a cholinesterase inhibitor.

Document D2 describes 2-amino-1-(4-chlorophenyl)-1,5-dihydro-5,5-diphenyl-4H-Imidazol-4-one (compound 5b).

Document D3 describes 3-methyl-5-phenyl-5-(5,6,7,8-tetrahydronaphthalen-2-yl)-2-thioxoimidazolidin-4-one.

Thus, a compound according to claims 1-6, 8-10, 15, 17-18, 20, 22-23, 30 and 34-35 is known from document D1. Furthermore, a compound according to claims 1-3, 5-6, 15, 17, 20 and 22 is known from document D2 and an intermediate compound according to claim 43 is known from document D3. The invention defined in claims 1-6, 8-10, 15, 17-18, 20, 22-23, 30, 34-35 and 43 is not new and consequently lacks novelty and inventive step.

The compounds according to claims 7, 11-14, 16, 19, 21, 24-29 differs from the compounds in D1 in the variation of the substituents.

Due to these features, new compounds are obtained.

Consequently, with the background of D1, the problem is to develop alternative imidazole derivatives that can be used in the treatment of cognitive and neurodegenerative diseases.

For a person skilled in the art it is obvious to make small changes in the structure to see if the new compounds can solve the stated problem.

.../...

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2006/001317

Supplemental Box

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

Continuation of: Box V

In order for a compound to be considered patentable, the difference must be shown to result in a novel and unexpected technical effect.

The compounds of the present invention are said to have improved properties (hERG selectivity) compared the compounds of D1.

However, it is considered unlikely that the whole scope of claims 7, 11-14, 16, 19, 21 and 24-29 has any unexpected or beneficial effects, compared to the previously known similar compounds, that they can be considered to differ essentially (Article 5,6 PCT) from said compounds.

The applicant has not indicated any difference in relation to prior art and the significance of such a difference for the whole of the scope of the claims.

As no other effect is presented in the present application, claims 7, 11-14, 16, 19, 21 and 24-29 lack an inventive step.

The cited prior art does not give any indication that would lead the person skilled in the art to claimed use of the intermediate compounds in the manufacture of a compound according to formula I (claim 44).

Accordingly, the invention defined in claim 44 is novel and is considered to involve an inventive step. The invention is industrially applicable.

Document D4-D7 discloses structurally related imidazole derivatives that are useful in the treatment of cognitive and neurodegenerative diseases but the documents are published after the claimed priority date and are not considered particularly relevant.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/SE2006/001317

Box No. VI Certain documents cited

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

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
US2005282825 A1, P	22/12/2005	15/06/2005	
US2006111370 A1, P	25/05/2006	09/06/2005	
WO2007005366 A1, E	11/01/2007	26/06/2006	
WO2007005404 A1, E	11/01/2007	26/06/2006	

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

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2006/001317

Box No. VII Certain defects in the international application

The following defects in the form or content of the international application have been noted:

Examples 215-246 in table 3 in the description lacks a generic structure that shows where the R''-group and R'''-group are attached.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/SE2006/001317

Box No. VIII Certain observations on the international application

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

The independent claim 29 comprises imidazole compounds as well as seven thioxoimidazoline compounds. These compounds are said to be active ingredients in a pharmaceutical formulation or used in the manufacture of a medicament to treat A-beta related pathologies such as Alzheimer's disease etc (claims 30 and 34-35). The two different groups of compounds in claim 29 should be separated into two claims to enhance the clarity of the claims.

The expression "A-beta related pathologies" in the second medical use claim 34 relates to a large and/or undefined number of different disorders which cannot be clearly defined by this expression. The application provides support for use of the compounds in the treatment of only a very limited number of such disorders. Claim 34 does therefore not meet the requirements of Article 6 PCT that claims shall be clear, concise and supported by the description.