

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/IB2015/052279	International filing date (day/month/year) 27.03.2015	Priority date (day/month/year) 10.04.2014
International Patent Classification (IPC) or both national classification and IPC INV. C07D513/04		
Applicant PFIZER INC.		

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.

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 Telephone No. +49 89 2399-0	
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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. 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>1-30</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-30</u>
Industrial applicability (IA)	Yes: Claims	<u>1-30</u>
	No: Claims	

2. Citations and explanations

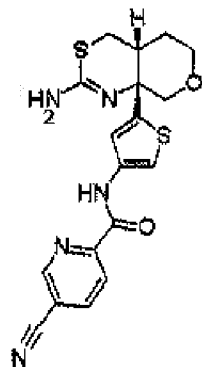
see separate sheet

Box No. VII Certain defects in the international application

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

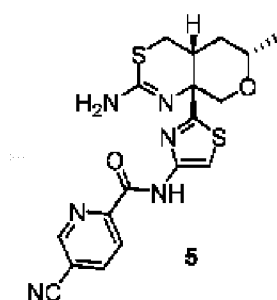
see separate sheet

- 2.3 However, since the latter are the result of a multiple selection in several lists of possible meaning of D1, they are novel over D1.
- 2.4 The structurally closest compound of D1 is described in example 64 (cpd 56, p.95) :



formula 56

Which differs for example from present compound 5



..., only by the absence of a methyl on tetrahydropyran ring and a thiophene ring instead of a thiazol.

However, D1 clearly encompasses these alternative substitution pattern (see for example p.79 (for the methyl) and paragraph [0027] for the definition of the 5-6 membered heteroaryl group (see "thiazolyl" I.33).

Compound 56 of D1 has been tested and shows a good inhibitory activity against Amiloid β production (see p.108, table 14, which is equivalent to Bace1 inhibition according to D1).

- 2.5 It is at present not seen what unexpected effects if any afford the compounds of the invention compared to the ones of D1, in particular compound 56.
- 2.6 A skilled person would have assumed that all the compounds enclosed in the scope of D1 exhibit the desired activity and selecting a particular domain of compounds as now claimed in present application, is merely one of several straightforward possibilities from which the skilled person would select, in

accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed, namely, providing alternative tetrahydropyrano-thyazin derivatives that are useful against neurodegenerative diseases.

- 3 Dependent claims 2-30 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.

Re Item VII

Certain defects in the international application

- 1 Independent claims 22-28, concerning individual compounds, comprise all the features of preceding claims and are therefore not appropriately formulated as claims dependent on the latter (Rule 6.4 PCT).
- 2 The closest prior art D1 should be cited and briefly commented (Rule 5.1(a)(ii) PCT).