


# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>REP0790WO</b>	<b>FOR FURTHER ACTION</b>	See Form PCT/PEA/416
International application No. <b>PCT/GB2006/002344</b>	International filing date ( <i>day/month/year</i> ) <b>27.06.2006</b>	Priority date ( <i>day/month/year</i> ) <b>28.06.2005</b>
International Patent Classification (IPC) or national classification and IPC <b>INV. C07D413/12</b>		
Applicant <b>Paradigm Therapeutics Ltd.</b>		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p style="margin-left: 20px;">a. <input type="checkbox"/> <i>sent to the applicant and to the International Bureau</i> a total of    sheets, as follows:</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p style="margin-left: 20px;">b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s))    , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I    Basis of the report</p> <p><input checked="" type="checkbox"/> Box No. II    Priority</p> <p><input type="checkbox"/> Box No. III    Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV    Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V    Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI    Certain documents cited</p> <p><input checked="" type="checkbox"/> Box No. VII    Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII    Certain observations on the international application</p>		
Date of submission of the demand  <b>2007-02-02</b>	Date of completion of this report  <b>04.12.2007</b>	
Name and mailing address of the international preliminary examining authority:   <b>European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465</b>	Authorized officer  <b>Helps, Ian</b>  Telephone No. <b>+49 89 2399-8209</b>	



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/GB2006/002344

---

**Box No. I Basis of the report**

---

1. With regard to the **language**, this report is based on
- 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 (under Rules 12.3(a) and 23.1(b))
    - publication of the international application (under Rule 12.4(a))
    - international preliminary examination (under Rules 55.2(a) and/or 55.3(a))
2. With regard to the **elements\*** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

**Description, Pages**

1-117 as originally filed

**Claims, Numbers**

1-24 as originally filed

a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3.  The amendments have resulted in the cancellation of:
- the description, pages
  - the claims, Nos.
  - the drawings, sheets/figs
  - the sequence listing (*specify*):
  - any table(s) related to sequence listing (*specify*):
4.  This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- the description, pages
  - the claims, Nos.
  - the drawings, sheets/figs
  - the sequence listing (*specify*):
  - any table(s) related to sequence listing (*specify*):
5.  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 70.2 (e)).

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/GB2006/002344

---

**Box No. II Priority**

---

1.  This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
  - translation of the earlier application whose priority has been claimed (Rule 66.7(b)).
2.  This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

---

**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

---

1. Statement

Novelty (N)	Yes: Claims	<u>1-24</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-24</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-24</u>
	No: Claims	

2. Citations and explanations (Rule 70.7):

**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**

---

**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**

## V. CITATIONS AND EXPLANATIONS

The following documents are mentioned in this Report.

EP-A-1,334,972	(A)
WO-A-2005 005442	(B)
WO-A-00 20358	(C)

The novel structural feature of the compounds of claim 1 is the presence of at least two heteroatoms in Ring 1, as well as the presence of the groups "Y" and "Z" on the phenyl group, which represent other than silicon containing groups. The dependent claims 2-15, as well as claim 16 drawn to compounds of claim 1 for use in therapy, claim 17 drawn to pharmaceutical compositions containing compounds of claim 1, and claims 18-24 drawn to the use of compounds of claim 1 for the preparation of medicaments are novel by consequence. Claims 1 to 24 therefore meet the Novelty requirements of Article 33(2) PCT.

The presently claimed compounds are useful as GnRH antagonists. Document (B) describes 2-(pyrimidin-4-yl)-aminocarbonyl-5-phenoxy-furans in which the phenyl group is substituted by a trialkyl silyl moiety (see examples). The compounds are useful as GnRH antagonists. Document (C) discloses several 2-phenylmethyl-5-(aryl- or heteroaryl)-aminocarbonyl-furans as GnRH antagonists. Further examples in which the heteroaryl group is pyrimidinyl are disclosed in document (A). The applicant has submitted comparative tests with the letter of 31.1.2007 which show that a representative compound of the present application shows better *in vitro* and *in vivo* GnRH inhibiting activity compared to compounds under the scope of document (B). Document (B) appears to be equally close prior art to documents (A) and (C) because the presently claimed compounds differ from those of (B) through the presence of a heteroaryl group containing two heteroatoms for "Ring 1", and the replacement of the trimethylsilyl group by t-butyl. In comparison with documents (A) and (C), the presently claimed compounds differ through the heteroaryl group "Ring 1" and the linkage "D", representing O or S. In view of these comparative tests, inventive step (Article 33(3) PCT) can be recognised because the problem of providing GnRH antagonists with improved activity has been solved in a non obvious manner.

**VII. CERTAIN DEFECTS IN THE INTERNATIONAL APPLICATION.**

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents (A) and (B) is not mentioned in the description, nor are these documents identified therein.

**VIII. CERTAIN OBSERVATIONS ON THE INTERNATIONAL APPLICATION.**

Due to the very broad scope of the substituents included in the definitions of "Ring 1", "Ring 2", E-G and J-L, it was not possible to carry out a complete structural search within a reasonable time. The structure search was therefore limited to the scope embraced by the worked examples (see Guidelines, B-III, 3.7). The PCT examination has therefore been limited to the searched subject matter.