Abstract:

A method of treating a movement abnormality associated with the pathology of a neurological movement disorder, such as Parkinson's disease or Restless Leg Syndrome by administering a therapeutically effective amount of a PDE7 inhibitory agent. An aspect of the invention provides for the administration of a PDE7 inhibitory agent in conjunction with a dopamine agonist or precursor, such as levodopa. In another aspect of the invention, the PDE7 inhibitory agent may be selective for PDE7 relative to other molecular targets (i) known to be involved with the pathology of Parkinson's disease or (ii) at which other drug(s) that are therapeutically effective to treat Parkinson's disease act.
INTERNATIONAL SEARCH REPORT

International application No
PCT/US 08/58530

According to International Patent Classification (IPC) or to both national classification and IPC

A CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/435 (2008.04)
USPC - 514/370

B FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8)- A61K 31/435 (2008 04)
USPC- 514/370

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC 549/181, 514/252 16

Biorganic & Medicinal Chemistry Letters Vol 14

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST (PGP8,USPT,EPAB,JPAB) PDE7, PDE, Parkinson, restless leg syndrome, neurologic, PLMS, levodopa, periodic limb movement in sleep, phosphodiesterase, dopa, bradykinesia, dopamine, esp@cenet pde7, parkinsons

Google Scholar PDE7, restless leg syndrome, g/mol, Parkinson

C DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
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<td>Y</td>
<td>US 2004/0162994 A1 (LEBEL et al) 19 Aug 2004 (19 08 2004), abstract, para [0013], [0015], [0016], [0038], [0039], [0060], [0063], [0070], [0079], [0085], [0088], [0095]</td>
<td>1-66</td>
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<td>Y</td>
<td>WO 2006/092691 A1 (COX et al) 8 Sep 2006 (08 09 2006), pg 1, in 4-6, pg 6, in 10-18, pg 7, in 3-20, pg 8, in 18-19, pg 34, In 4-6, pg 42, In 17-18, pg 45, In 9-10, pg 46, In 21-23, 31-36, pg 84, In 3-6, pg 89, In 34 to pg 90, In 4</td>
<td>1-25, 28, 30-66</td>
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<td>Y</td>
<td>US 2005/0148604 A1 (INOUE et al) 7 Jul 2005 (07 07 2005), abstract, para [0111], pg 49, pg 57</td>
<td>26, 27, 62, 63</td>
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<td>Y</td>
<td>US 2003/0045557 A1 (VERGNE et al) 4 Mar 2003 (04 03 2003), abstract, para [0036], [0691], pg 93, pg 108</td>
<td>29, 65</td>
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</tbody>
</table>

Further documents are listed in the continuation of Box C

D

* Special categories of cited documents
**A** document defining the general state of the art which is not considered to be of particular relevance
**B** earlier application or patent but published on or after the international filing date
**L** document which may throw doubts on the novelty of the claimed invention 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
11 September 2008 (07 09 2008)

Date of mailing of the international search report
18 SEP 2008

Authorized officer
Lee W Young

PCT Mail/Incn: 571-272-4300
PCTOSP 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)
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### INTERNATIONAL SEARCH REPORT

**International application No**

PCT/US 08/58530

#### 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 64(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

- **Group I**: claims 1-26, 39-62, 66, drawn to a method of treating a movement abnormality associated with the pathology of a neurological movement disorder comprising administering to a patient an amount of a PDE7 inhibitory agent effective to inhibit the enzymatic activity of PDE7

- **Group II**: claims 1-25, 27, 39-61, 63, 66, drawn to a method of treating a movement abnormality associated with the pathology of a neurological movement disorder comprising administering to a patient an amount of a PDE7 inhibitory agent effective to inhibit the enzymatic activity of PDE7

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**See SUPPLEMENTAL SHEET TO CONTINUE**

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1. **A** as all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims

2. **A** as all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees

3. **A** 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

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

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2007)
Box III - Continuation of Lack of Unity

Group III, claims 1-25, 28, 39-61, 64, 66, drawn to a method of treating a movement abnormality associated with the pathology of a neurological movement disorder comprising administering to a patient in need thereof an amount of a PDE7 inhibitory agent effective to inhibit the enzymatic activity of PDE7

Group IV, claims 1-25, 29, 39-61, 65, 66, drawn to a method of treating a movement abnormality associated with the pathology of a neurological movement disorder comprising administering to a patient in need thereof an amount of a PDE7 inhibitory agent effective to inhibit the enzymatic activity of PDE7

Group V, claims 30-38, drawn to a method for identifying an agent that inhibits PDE7 activity useful for treating a movement abnormality associated with the pathology of a neurological movement disorder in a mammalian subject

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13 1 because, under PCT Rule 13 2, they lack the same or corresponding special technical features for the following reasons:

As to Groups I-V, Groups I-IV do not include the inventive concept of identifying an agent that inhibits PDE7 activity, as required by Group V.

As to Groups I-IV, said groups would be regarded as having the same or corresponding technical feature if the compounds of claims 26/62, 27/63, 28/64, and 29/65 had a common property or activity, and shared a significant structural element that is essential to the common property or activity. While said compounds do share the common property of inhibiting PDE7 activity, they do not share a significant structural element that is an improvement over the prior art. In addition, the article entitled "Discovery of thiadiazoles as a novel structural class of potent and selective PDE7 inhibitors Part 1 Design, synthesis and structure-activity relationship studies" by Vergne et al. (Bioorganic & Medicinal Chemistry Letters 2004, 14 4607-4613) teaches the compound of claims 29/65 that selectively inhibits PDE7 (compound 48, Table 3, pg 4611) Thus, there is no same or corresponding technical feature and unity of invention is lacking.

Groups I-V therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.