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(71) Applicants (for all designated States except US): **SCHERING CORPORATION** [US/US]; 2000 Galloping Hill Road, Kenilworth, NJ 07033-0530 (US). **PHARMA-COPEIA DRUG DISCOVERY, INC.** [US/US]; 3000 Eastpark Boulevard, Cranbury, NJ 08512 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ZHU, Zhaoning** [US/US]; 6 Cypress Court, Plainsboro, NJ 08536 (US). **MCKITTRICK, Brian** [US/US]; 14 Millbrook Road, New Vernon, NJ 07976 (US). **SUN, Zhong-Yue** [CN/US]; 12 Straton Court, Parlin, NJ 08859 (US). **YE, Yuanzan, C.** [CN/US]; 103 Othen Street, Edison, NJ 08817 (US). **VOIGT, Johannes, H.** [DE/US]; 10 Willow Street, Cranford, NJ 07016 (US). **STRICKLAND, Corey** [US/US]; 825 Newmans Lane, Martinsville, NJ 08836 (US). **SMITH, Elizabeth, M.** [CA/US]; 166 Grove Street, Verona, NJ 07044 (US). **STAMFORD, Andrew** [AU/US]; 27 Overlook Road, Chatham Township, NJ 07928 (US). **GREENLEE, William, J.** [US/US]; 115 Herrick Avenue, Teaneck, New Jersey 07666 (US). **MAZZOLA, Robert** [US/US]; 6 Greenwich Church Road, Stewartsville, NJ 08886 (US). **CALDWELL, John** [US/US]; 86 Upper

Lakeview Avenue, Ringwood, NJ 07456 (US). **CUM-MING, Jared** [US/US]; 417 Center Street, Garwood, New Jersey 07027 (US). **WANG, Lingyan** [CN/US]; 41 Cortland Drive, East Brunswick, NJ 08816 (US). **WU, Yusheng** [US/US]; 235 East 40th Street, Apt. 20C, New York, NY 10016 (US). **ISERLOH, Ulrich** [DE/US]; 1110 Park Avenue, Apt. 2L, Hoboken, NJ 07030 (US). **GUO, Tao** [US/US]; 1606 Dahlia Circle, Dayton, NJ 08810 (US). **LE, Thuy, X., H.** [US/US]; 16 Black Gum Drive, Monmouth Junction, NJ 08852 (US). **SAIONZ, Kurt, W.** [US/US]; 508 Linden Place, Cranford, NJ 07016 (US). **BABU, Suresh, D.** [US/US]; 1407 Aspen Drive, Plainsboro, NJ 08536 (US). **HUNTER, Rachael, C.** [GB/US]; 27 Chestnut Street, Princeton, NJ 08542 (US). **MORRIS, Michelle, L.** [US/US]; 10 Carla Way, Lawrenceville, NJ 08648 (US). **GU, Huizhong** [US/US]; 22 Cotoneaster Court, Monmouth Junction, NJ 08852 (US). **QIAN, Gang** [CN/US]; 59 Colleen Court, Kendall Park, NJ 08824 (US). **TADESSE, Dawit** [US/US]; U-15 Avon Drive, East Windsor, NJ 08520 (US).

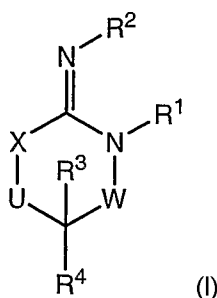
(74) Agent: **LEE, William, Y.**; SCHERING-PLOUGH CORPORATION, Patent Department, K-6-1 1990, 2000 Galloping Hill Road, Kenilworth, NJ 07033-0530 (US).

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[Continued on next page]

(54) Title: HETEROCYCLIC ASPARTYL PROTEASE INHIBITORS



(I)

(57) Abstract: Disclosed are compounds of the formula (I) or a stereoisomer, tautomer, or pharmaceutically acceptable salt or solvate thereof, and pharmaceutical compositions comprising the compounds of formula (I). Also disclosed is the method of inhibiting aspartyl protease, and in particular, the methods of treating cardiovascular diseases, cognitive and neurodegenerative diseases, and the methods of inhibiting of Human Immunodeficiency Virus, plasmepsins, cathepsin D and protozoal enzymes. Also disclosed are methods of treating cognitive or neurodegenerative diseases using the compounds of formula (I) in combination with a cholinesterase inhibitor or a muscarinic m₁ agonist or m₂ antagonist.

**Declarations under Rule 4.17:**

- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*

Published:

- *with international search report*

(88) Date of publication of the international search report:
25 January 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/020446

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/4168 A61K31/4178 C07D233/46 C07D233/88 C07D239/22
C07D271/06 C07D273/00 C07D401/10 C07D403/06 C07D403/12
C07D407/10 C07D409/04 C07D409/14 C07D413/10 C07D413/12

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)

C07D

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 practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 2005/058311 A (SCHERING CORPORATION; PHARMACOPEIA DRUG DISCOVERY, INC; ZHU, ZHAONING;) 30 June 2005 (2005-06-30) see examples	1-15
A	WO 90/04917 A (ABBOTT LABORATORIES) 17 May 1990 (1990-05-17) abstract; claim 1	1-15

☒ 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 document 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.

* & * document member of the same patent family

Date of the actual completion of the international search

12 July 2006

Date of mailing of the international search report

26/07/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bérillon, L

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/020446

Box 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.: 3-6, 8-13, 15
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 3-6, 8-13 and 15 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 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:

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 any additional fee.
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.:
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.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2005/020446

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2005058311	A	30-06-2005	AR 047050 A1	04-01-2006
WO 9004917	A	17-05-1990	AU 4849390 A	28-05-1990
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