

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
7 September 2007 (07.09.2007)

PCT

(10) International Publication Number
WO 2007/100351 A3

(51) International Patent Classification:

C07D 309/30 (2006.01) **C07F 7/18** (2006.01)
C07C 235/30 (2006.01)

(21) International Application Number:

PCT/US2006/035824

(22) International Filing Date:

13 September 2006 (13.09.2006)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/717,006 13 September 2005 (13.09.2005) US
60/742,541 6 December 2005 (06.12.2005) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:

6 December 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.

(54) Title: PROCESS FOR PREPARING SIMVASTATIN AND INTERMEDIATES THEREOF

(57) Abstract: Novel processes for the preparation of simvastatin and intermediates of such processes. Preferred embodiments include the preparation of lovastatin amides, protected lovastatin amide derivatives, simvastatin dihydroxy acid amide derivatives, alkali salts, simvastatin dihydroxy acids, simvastatin ammonium salts, and simvastatin.



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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/035824

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D309/30 C07C235/30 C07F7/18

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 C07C C07F

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, BEILSTEIN Data, 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.
X	WO 03/045935 A (FERMIC S A DE C V [MX]; GALEAZZI EDVIGE [MX]; GARCIA GUSTAVO A [MX]; L) 5 June 2003 (2003-06-05) page 14; claims 1-26 -----	1-48
X	WO 2005/066150 A (HETERO DRUGS LTD [IN]; PARTHASARADHI REDDY BANDI [IN]; RATHNAKAR REDDY) 21 July 2005 (2005-07-21) page 5, line 8 - page 8, line 5; claims 1-12 -----	1-48
X	US 4 820 850 A (VERHOEVEN THOMAS R [US] ET AL) 11 April 1989 (1989-04-11) column 3, line 28 - column 5, line 8; claim 1; example 1 -----	1-48



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
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- *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

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- *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

18 September 2007

Date of mailing of the international search report

26/09/2007

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/035824

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.:
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 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:

see additional sheet

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-21

subject-matter relating to the transformation of II (or VII) into III, wherein the molar ratio of the amine to the lovastatin compound is no more than 1.5 (as defined in claim 1)

2. claims: 9-31, 38-44

subject-matter relating to the transformation of III into IV, wherein a silylation catalyst is present.

3. claims: 32-44

subject-matter relating to the transformation of IV into V, wherein an amine derivative is added to compound IV before the alkyllithium and/or alkali hydride is added.

4. claims: 45-48

subject-matter relating to compounds of formula IVa (and its transformation into I).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/035824

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