UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

NOTICE OF ALLOWANCE AND ISSUE FEE DUE

CORRECTED COPY

020914 HM12/1019
MARLA J MATHIAS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON NJ 08543-4000

APPLICATION NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT		DATE MAILED
09/788,173	02/16/01	024	GERSTL, R	1626	10/19/01
First Named Applicant	ROBL,		35 USC 154(b) term ext. =	0 Days.	

TITLE OF INVENTION: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEE DUE	DATE DUE
1 LA0050 NP	514-412.000	N53	UTILITY	NO	$1280.00	01/22/02

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED.

THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.

HOW TO RESPOND TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.
If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or
B. If the status is the same, pay the FEE DUE shown above.

If the SMALL ENTITY is shown as NO:

A. Pay FEE DUE shown above, or

B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.

II. Part B-Issue Fee Transmittal should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by charge to deposit account, Part B Issue Fee Transmittal should be completed and returned. If you are charging the ISSUE FEE to your deposit account, section "4b" of Part B-Issue Fee Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give application number and batch number.
Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

EXHIBIT
Ex. 1005
Part 2

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PATENT AND TRADEMARK OFFICE COPY

Notice of Allowability

Application No.	Applicant(s)
09/788,173	Robl
Examiner	**Art Unit**
Robert Gerstl	1626

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *8/31/01*.

2. ☒ The allowed claim(s) is/are *1-24*.

3. ☐ The drawings filed on _____ are acceptable as formal drawings.

4. ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____.
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   *Certified copies not received: _____.

5. ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE FOR SUBMITTING NEW FORMAL DRAWINGS, OR A SUBSTITUTE OATH OR DECLARATION.** ~~This three-month period for complying with the REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL is extendable under 37 CFR 1.136(a).~~

6. ☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

7. ☐ Applicant MUST submit NEW FORMAL DRAWINGS

   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
   1) ☐ hereto or 2) ☐ to Paper No. _____.

   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the examiner.

   (c) ☐ including changes required by the attached Examiner's Amendment/Comment or in the Office action of Paper No. _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

8. ☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any reply to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

1 ☐ Notice of References Cited (PTO-892)
2 ☐ Notice of Informal Patent Application (PTO-152)
3 ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
4 ☐ Interview Summary (PTO-413), Paper No. _____.
5 ☒ Information Disclosure Statement(s) (PTO-1449), Paper No(s). 2
6 ☐ Examiner's Amendment/Comment
7 ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
8 ☐ Examiner's Statement of Reasons for Allowance
9 ☐ Other

ROBERT GERSTL
PRIMARY EXAMINER
ART UNIT 1626

FORM PTO-1449 (REV. 7-85)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

ATTY. DOCKET NO.
LA0050 NP
APPLICATION NO.
09/788,173
APPLICANT
ROBL ET AL.
FILING DATE
FEBRUARY 16, 2001
Group

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE
	AA	5,462,928	10/31/95	Bachovchin et al			
	AB	5,939,560	8/17/99	Jenkins et al			
	AC	6,011,155	1/4/00	Villhauer, E.B.			
	AD	6,110,949	8/29/00	Villhauer, E.G.			
	AE						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	OFFICE	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	AF	WO 97/40832	11/6/01	PCT			☐	☐
	AG	WO 99/38501	8/5/99	PCT			☐	☐
	AH	WO 99/67279	12/29/99	PCT			☐	☐
	AI	WO 00/10549	3/2/00	PCT			☐	☐
	AJ	WO 00/53171	9/14/00	PCT			☐	☐
	AK	WO 00/56296	9/28/00	PCT			☐	☐
	AL	WO 00/56297	9/28/00	PCT			☐	☐
	AM	WO 00/69868	11/23/00	PCT			☐	☐
	AN	EP 1050540A2	11/8/00	Europe			☐	☐
	AO	WO 034241A1	6/15/00	PCT			☐	☐
	AP						☐	☐

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent pages, Etc.)

	AQ	Lin, J. et al, Proc. Natl. Acad. Sci, USA, Vol. 95, pp. 14020-14024, Nov. 1998
	AR	Augustyns, KJL et al, Eur. J. Med. Chem. 32, 301-309, (1997)
	AS	Hughes, T.E. et al, Biochemistry, 28, 11597-11603, 1999

EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609: Draw a line through citation if not in conformance and not considered. Include a copy of this form with the next communication to applicant.

FORM PTO-1449 (REV. 7-85)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

ATTY. DOCKET NO.
LA0050 NP
APPLICATION NO.
09/788,173
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ROBL ET AL.
FILING DATE
FEBRUARY 16, 2001

Group

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent pages, Etc.)

	AT	Yamada, M. et al, Bioorganic & Medicinal Chemistry Letters 8, 1537-1540 (1998)
	AU	Tanaka, S. et al, Immunopharmacology 40, 21-26 (1998)
	AV	Li, J. et al, Archives of Biochemistry and Biophysics, Vol. 323, No. 1, pp. 148-154, Oct. 20, 1995
	AW	Ashworth, D.M. et al, Bioorganic & Medicinal Chemistry Letter, Vol. 6, No. 22, pp. 2745-2748, 1996
	AX	Yamada, M. et al, Bioorganic & Medicinal Chemistry Letter 8, 1537-1540 (1998)
	AY	Ashworth, D.M. et al, Bioorganic & Medicinal Chemistry Letter, Vol. 6, No. 10, pp. 1163-1166, 1996
	AZ	Lambeir, A.-M., et al, Biochimica et Biophysica Acts, 1290, pp. 76-82 (1996)
	BA	Yoshimoto, T. et al, Agric. Biol. Chem., 55(4), pp. 1135-1136, 1991
	BB	Belyaev, A. et al, J. Med. Chem., 42, 1041-1052, 1999
	BC	Stockel, A. et al, Peptides: Chemistry, Structure and Biology, pp. 709-710, 1996
	BD	Asai, Y. et al, The Journal of Antibiotics, Vol. 50, No. 8, pp. 653-657, Aug. 1997
	BE	Demuth, H.-U. et al, FEBS LETTERS, Vol. 320, No. 1, pp. 23-27, March 1993
	BF	Ohnuki, T. et al, Drugs of the Future, 24(6): 665-670, 1999
	BG	Demuth, H-U. et al, Diabetes, 2000, Vol. 49, suppl. 1, A102
	BH	Rotherberg, P. et al, Diabetes, 2000, Vol. 49, Suppl. 1, A39

CASE LA0050 NP

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Burton Rodney — Type or print name

Signature

Nov. 5, 2001 — Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

ROBL ET AL.

APPLICATION NO: 09/788,173

FILED: FEBRUARY 16, 2001

FOR: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

Art Unit: 1626

Examiner: R. Gerstl

Batch No.: N53

Assistant Commissioner for Patents
Washington, D.C. 20231

PETITION PURSUANT TO 37 CFR §1.97(d)

Sir:

Consideration of the Information Disclosure Statement submitted concurrently herewith is requested. Please charge Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company in the amount of $180 for payment of the fee for filing this petition.

An additional copy of this paper is here enclosed. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,

Burton Rodney
Attorney for Applicants
Reg. No. 22,076

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336
Date: Nov. 5, 2001

CASE LA0050 NP

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Burton Rodney		Nov. 5, 2001
Type or print name	Signature	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

ROBL ET AL.

APPLICATION NO: 09/788,173

FILED: FEBRUARY 16, 2001

Art Unit: 1626

Examiner: R. Gerstl

Batch No.: N53

FOR: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

Assistant Commissioner for Patents
Washington, D.C. 20231

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

In accordance with 37 C.F.R. §1.56, applicants wish to call the Examiner's attention to the references cited on the attached form(s) PTO-1449.

These references were cited in a search report in a corresponding PCT International application dated October 23, 2001 that is within 3 months of the filing of this information disclosure statement. Copies of these references and the search report are enclosed herewith.

A petition pursuant to 37 C.F.R. §1.97(d) is enclosed herewith.

The Examiner is requested to consider the foregoing information in relation to this application and indicate that each reference was considered by returning a copy of the initialed PTO 1449 form(s).

12/21/2001 CCHAU1 00000059 193880 09788173
01 FC:126 180.00 CH

Certificate under 37 C.F.R. §1.97(e)(1)

I, the undersigned attorney, hereby certify that each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement.

Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336

Date: Nov. 5, 2001

Burton Rodney
Attorney for Applicants
Reg. No. 22,076

Best Available Copy

FORM PTO-1449 (REV. 7-85)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

ATTY. DOCKET NO.
LA0050 NP
APPLICATION NO.
09/788,173
APPLICANT
ROBL ET AL.
FILING DATE
FEBRUARY 16, 2001

Group
1626

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE
	AA	4,254,057	3/3/81	Day et al			
	AB	4,379,785	4/12/83	Weyer et al			
	AC	5,998,463	12/7/99	Hulin et al			
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	OFFICE	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	AL	EP 0 007 652A1	2/6/80	EP			☐	☐
	AM	DE 33 24 263 A1	1/17/85	German			☐	☐
	AN	EP 0 219 782 A2	4/29/87	EP			☐	☐
	AO	DE 39 26 606 A1	2/14/91	German			☐	☐
	AP	WO 99/26659	6/3/99	PCT			☐	☐
	AQ	WO 99/47545	9/23/99	PCT			☐	☐

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent pages, Etc.)

AR	Sagnard, I. et al, Tetrahedron Letters, Vol. 36, No. 18, pp. 3149-3152, 1995.
AS	Tverezovsky, V.V. et al, Tetrahedron, Vol. 53, No. 43, pp. 14773-14792, 1997.
AT	Hanessian, S. et al, Bioorganic & Medicinal Chem. Letters, Vol. 8, No. 16, pp. 2123-2128, Aug. 18, 1998.

EXAMINER | **DATE CONSIDERED**

*EXAMINER: Initial of reference considered, whether or not citation is in conformance with MPEP 609. Draw a line through citation if not in conformance and not considered. Include a copy of this form with the next communication to applicant.

Best Available Copy

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
BRISTOL-MYERS SQUIBB CO.
Attn. Algieri, Aldo A.
P.O. Box 4000
Lawrenceville-Princeton Rd
PRINCETON, NJ 08543
UNITED STATES OF AMERICA

Applicant's or agent's file reference LA0050	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 01/07151	International filing date *(day/month/year)* 05/03/2001
Applicant BRISTOL-MYERS SQUIBB CO.	Date of mailing *(day/month/year)* 23/10/2001

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority 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 Chantal Meyer

Form PCT/ISA/220 (July 1998)

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international pbulication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
LA0050		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 01/ 07151	05/03/2001	10/03/2000
Applicant		
BRISTOL-MYERS SQUIBB CO.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL IV, PROCESSES FOR THEIR PREPARATION, AND THEIR USE

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[ ] None of the figures.

Form PCT/ISA/210 (first sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/07151

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D209/52 A61K31/403 A61P3/04 A61P3/06 A61P3/10

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)
IPC 7 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, 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.
Y	US 6 011 155 A (VILLHAUER EDWIN BERNARD) 4 January 2000 (2000-01-04) abstract; claims; examples	1-7,11, 23,24
Y	WO 99 47545 A (WANNAMAKER MARION W; BEMIS GUY W (US); MURCKO MARK A (US); VERTEX) 23 September 1999 (1999-09-23) page 9, formula I; page 26, especially lines 18-22; page 97, compounds 23d, 23h claims 1,6,18,19,23	1-7,11, 23,24
A	WO 99 67279 A (SCHMIDT JOERN; GLUND KONRAD (DE); DEMUTH HANS ULRICH (DE); HOFFMAN) 29 December 1999 (1999-12-29) page 11 -page 17; claims 1,2,8-13	1,11-13, 22-24

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in 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	Date of mailing of the international search report
16 October 2001	23/10/2001

Name and mailing address of the ISA	Authorized officer
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	Hass, C

1

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 379 785 A (WEYER RUDI ET AL) 12 April 1983 (1983-04-12) cited in the application claims 1,5,6	1,11,23, 24
A	EP 0 219 782 A (HOECHST AG) 29 April 1987 (1987-04-29) page 1, formula (I); page 3, substructure K; page 16, line 33 to page 17, line 6 claims 1,2	1,11,23
A	DE 33 24 263 A (HOECHST AG) 17 January 1985 (1985-01-17) claims 1,19,20	1,11
A	DE 39 26 606 A (HOECHST AG) 14 February 1991 (1991-02-14) page 2, formula (I); page 3, substructure (K); page 6, lines 62-66	1
A	US 4 254 057 A (DAY JANET A ET AL) 3 March 1981 (1981-03-03) column 2, line 26 - line 38	1
A	EP 0 007 652 A (SHELL INT RESEARCH) 6 February 1980 (1980-02-06) claim 1	1
A	HANESSIAN S ET AL: "Probing the Importance of Spacial and Conformational Domains in Captopril Analogs for Angiotensin Converting Enzyme Activity" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 8, no. 16, 18 August 1998 (1998-08-18), pages 2123-2128, XP004137231 ISSN: 0960-894X the whole document	1
A	TVEREZOVSKY V V ET AL: "Synthesis of (2S, 3R, 4S)-3,4-Methanoproline and Analogues by Cyclopropylidene Insertion" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 53, no. 43, 27 October 1997 (1997-10-27), pages 14773-14792, XP004106307 ISSN: 0040-4020 the whole document	1

-/--

1

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	SAGNARD I ET AL: "Enantioselective Synthesis of Cyclopropane alpha-Amino Acids: Synthesis of N-Boc-cis-(2S,3R,4S)-3,4-Methanoproline and N-Boc-(2S,3R,4S)-3,4-Methanoglutamic Acid" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 36, no. 18, 1 May 1995 (1995-05-01), pages 3149-3152, XP004028212 ISSN: 0040-4039 the whole document ---	1
A	WO 99 26659 A (HOOVER DENNIS JAY; TREADWAY JUDITH LEE (US); HULIN BERNARD (US); P) 3 June 1999 (1999-06-03) cited in the application claims 1,6,7 ---	12-14, 22-24
A	US 5 998 463 A (HULIN BERNARD ET AL) 7 December 1999 (1999-12-07) cited in the application claims 1,22,23 -----	12-14, 22,23

1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/07151

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 23, 24 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 II Observations where unity of invention is lacking (Continuation of item 2 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/US 01/07151

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		WO 9926659 A1	03-06-1999
		NO 20002164 A	19-07-2000
		PL 340643 A1	12-02-2001
US 5998463 A	07-12-1999	NONE	

B

CASE LA0050 NP

5

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Burton Rodney		Nov. 14, 2001
Type or print name	Signature	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

ROBL ET AL.

Art Unit: 1626

Examiner: R. Gerstl

Match and Return

APPLICATION NO: 09/788,173

FILED: FEBRUARY 16, 2001

FOR: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

8/B
Harmon
4/16/02

Assistant Commissioner for Patents
Box Issue Fee
Washington, D.C. 20231

OK 3/11

AMENDMENT UNDER 37 CFR 1.312

Sir:

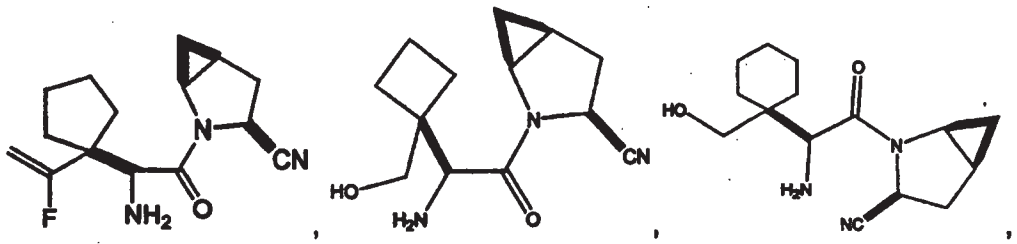
Please amend the above-identified application to read as follows:

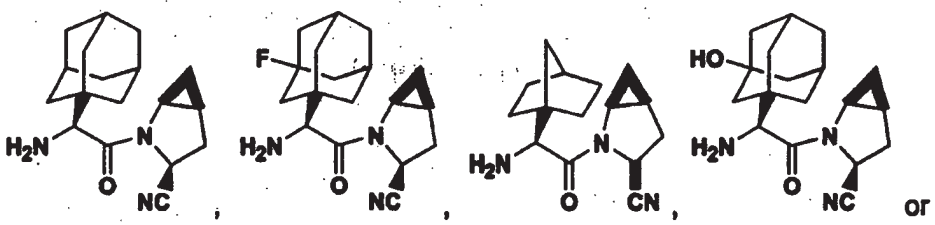
In the Claims:

Please amend Claims 8 and 10 to read as follows:

B1

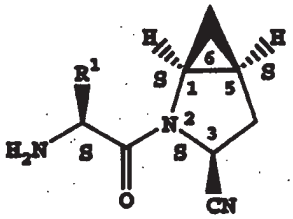
8. (Amended) A compound having the structure:





or a pharmaceutically acceptable salt thereof.

10. (Amended) A compound which is

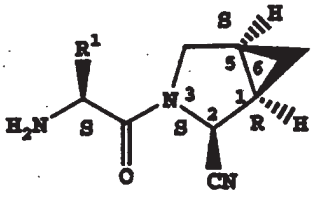


A

(1S,2(2S),3S,5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R,2S,3(2S),5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl.

Remarks

Claims 1 to 24 are present and have been allowed in the Notice of Allowance mailed October 19, 2001.

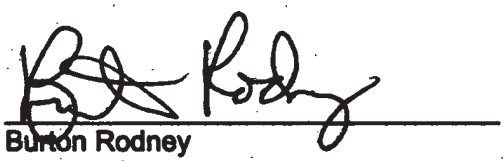
As seen above, Claims 8 and 10 have been amended to place each in independent form. No new matter has been added.

It is respectfully requested that the above amendments be entered.

A copy of Claims 8 and 10 with markings to show changes made is attached.

It is believed that this application is now in condition for issuance once the final fee has been paid.

Respectfully submitted,



Burton Rodney
Attorney for Applicants
Reg. No. 22,076

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336

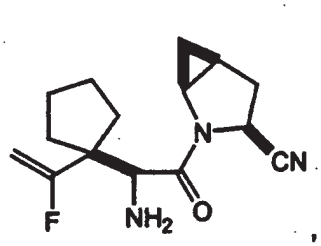
Date: Nov. 14, 2001

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 8 and 10 have been amended as follows:

-- 8. (Amended) [The] A compound [as defined in Claim 1] having the structure:



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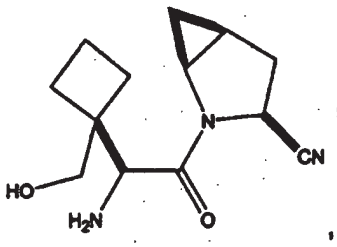

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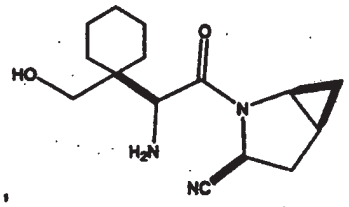

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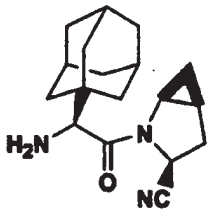

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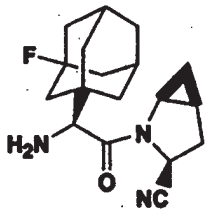

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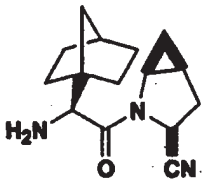

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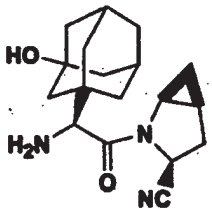
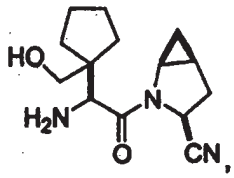


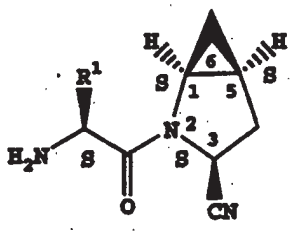
or



,

or a pharmaceutically acceptable salt thereof.--

--10. (Amended) [The] A compound [as defined in Claim 1] which is

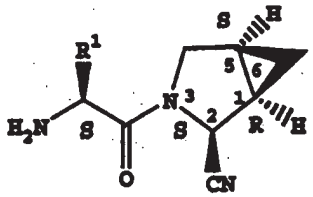


A

(1S,2(2S),3S,5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R,2S,3(2S),5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl. --

PART B—ISSUE FEE TRANSMITTAL

Complete and mail this form, together with applicable fees, to: **Box ISSUE FEE**
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B#

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Burton Rodney (Depositor's name)
(Signature)
Jan. 15, 2002 (Date)

APPLICATION NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT		DATE MAILED
09/788,173	02/16/01	024	GERSTL, R	1626	10/19/01

First Named Applicant: ROBL, — 35 USC 154(b) term ext. = 0 Days.

TITLE OF INVENTION: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEE DUE	DATE DUE
1 LA0050 NP	514-412.000	N53	UTILITY	NO	$1280.00	01/22/02

1. Change of correspondence address or indication of " Fee Address" (37 CFR 1.363). Use of PTO form(s) and Customer Number are recommended, but not required.

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☒ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47) attached.

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Burton Rodney
2
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)
PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the PTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE
Reel: 011607
Frame: 0369
Bristol-Myers Squibb Company

(B) RESIDENCE: (CITY & STATE OR COUNTRY)
Princeton, New Jersey

Please check the appropriate assignee category indicated below (will not be printed on the patent)

☐ Individual ☒ corporation or other private group entity ☐ government

4a. The following fees are enclosed (make check payable to Commissioner of Patents and Trademarks):

☐ Issue Fee
☐ Advance Order - # of Copies _____

4b. The following fees or deficiency in these fees should be charged to:

DEPOSIT ACCOUNT NUMBER 19-3880
(ENCLOSE AN EXTRA COPY OF THIS FORM)

☒ Issue Fee
☐ Advance Order - # of Copies _____

The COMMISSIONER OF PATENTS AND TRADEMARKS IS requested to apply the Issue Fee to the application identified above.

(Authorized Signature) (Date) 1/15/02

NOTE; The Issue Fee will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the Patent and Trademark Office.

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending on the needs of the individual case. Any comments on the amount of time required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND FEES AND THIS FORM TO: Box Issue Fee, Assistant Commissioner for Patents, Washington D.C. 20231

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

09788173
02/11/2002 CV0222 00000005 193880
1280.00 CH
01 FC:142

TRANSMIT THIS FORM WITH FEE

3

B#

CASE LA0050 NP

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Burton Rodney
Type or print name

Signature

January 15, 2002
Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF
ROBL ET AL.
APPLICATION NO: 09/788,173
FILED: FEBRUARY 16, 2001
FOR: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

Art Unit: 1626
Examiner: R. Gerstl
Batch No.: N53

Box Issue Fee
Commissioner for Patents
Washington, D.C. 20231

OK to Enter

RESPONSE TO NOTICE OF PUBLICATION FEE DUE

Sir:

This is in response to the Notice of Publication Fee Due, dated November 14, 2001, a reply to which is due February 14, 2002.

Please charge Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company in the amount of $300.00 for the publication fee due. An additional copy of this paper is herewith enclosed. The Commissioner is hereby authorized to charge any additional fees under 37 CFR §1.17 which may be required, or credit any overpayment, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

If this application is not published, Applicants request a refund of the publication fee paid, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336

Burton Rodney
Attorney for Applicants
Reg. No. 22,076

Date: Jan. 15, 2002

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. 20231
www.uspto.gov

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
09/788,173	02/1[illegible]/2001	Jeffrey A. Robl	LA0050 NP

CONFIRMATION NO. 4018

OC000000007068445

23914
MARLA J MATHIAS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

Title: Cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV and method

Date Mailed: 11/14/2001

NOTICE OF PUBLICATION FEE DUE

The above-identified application was filed (including as a Continued Prosecution Application) on or after November 29, 2000 and a non-publication request in compliance with 37 CFR 1.213 was not included with the application on filing. Since the application has been allowed, a publication fee is due.

The fee due is $300.00. No small entity discount is available. See 37 CFR 1.18(d).

The reply to this notice should be mailed to:
Box ISSUE FEE
Commissioner for Patents
Washington D.C. 20231.

The publication fee must be submitted within **THREE MONTHS** from the mailing date of this notice or the application may be regarded as abandoned. No extensions of time under 37 CFR 1.136(a) or (b) are available. A reply must be filed to this notice, even if applicant does not anticipate that the application will be published (e.g., because the patent has issued and the projected publication date is more than a month after the issue date of the patent). A proper reply to this notice in such a situation would be a statement that no fee is now due, citing 37 CFR 1.211(e). If publication of the application does not occur, any publication fee paid will be refunded, if applicant requests a refund. See 37 CFR 1.211(e).

Questions relating to this Notice should be directed to the Office of Patent Publication at (703) 305-8283.

A copy of this notice should be returned with any reply.

02/11/2002 CV0222 00000006 193880 09788173
01 FC:195 300.00 CH

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,173	02/16/2001	Jeffrey A. Robl	LA0050 NP	4018

23914 7590 04/01/2002

STEPHEN B. DAVIS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER	
GERSTL, ROBERT	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 04/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Response to Rule 312 Communication	Application No.	Applicant(s)	
	09/788,173	ROBL ET AL.	
	Examiner	Art Unit	
	Robert Gerstl	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

1. ☒ The amendment filed on *12/20/01* under 37 CFR 1.312 has been considered, and has been:

   a) ☐ entered.

   b) ☒ entered as directed to matters of form not affecting the scope of the invention.

   c) ☐ disapproved because the amendment was filed after the payment of the issue fee.
   Any amendment filed after the date the issue fee is paid must be accompanied by a petition under 37 CFR 1.313(c)(1) and the required fee to withdraw the application from issue.

   d) ☐ disapproved. See explanation below.

   e) ☐ entered in part. See explanation below.

Robert Gerstl
Primary Examiner
Art Unit: 1626

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,173	02/16/2001	Jeffrey A. Robl	LA0050 NP	4018

23914 7590 04/18/2002

STEPHEN B. DAVIS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER	
GERSTL, ROBERT	
ART UNIT	**PAPER NUMBER**
1626	9

DATE MAILED: 04/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Response to Rule 312 Communication	Application No.	Applicant(s)	
	09/788,173	ROBL ET AL.	
	Examiner	Art Unit	
	Robert Gerstl	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

1. ☒ The amendment filed on *1/2/02* under 37 CFR 1.312 has been considered, and has been:

   a) ☐ entered.

   b) ☒ entered as directed to matters of form not affecting the scope of the invention.

   c) ☐ disapproved because the amendment was filed after the payment of the issue fee.
   Any amendment filed after the date the issue fee is paid must be accompanied by a petition under 37 CFR 1.313(c)(1) and the required fee to withdraw the application from issue.

   d) ☐ disapproved. See explanation below.

   e) ☐ entered in part. See explanation below.

Robert Gerstl
Primary Examiner
Art Unit: 1626

CASE LA0050 NP

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Burton Rodney	B Rodney	June 22, 2004
Type or print name	Signature	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

ROBL ET AL.

PATENT NO.: 6,395,767

ISSUED: MAY 28, 2002

FOR: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

Certificate
JUN 29 2004
of Correction

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
ATTENTION: Decision and Certificate of Correction
Branch of Patent Issue Division

REQUEST FOR CERTIFICATE OF CORRECTION OF PATENT
FOR PTO MISTAKE (37 C.F.R. §1.322(a))

Sir:

Attached, in duplicate, is PTO/SB/44 (also Form PTO-1050), with at least one copy being suitable for printing.

The exact page and line number where the errors are shown correctly in the application file are:

Claim 8 should read: --A compound having the structure:--.

Claim 10 should read: --A compound which is--.

This correction is necessary because of an error by the Office as follows.

Applicants filed an AMENDMENT UNDER 37 CFR 1.312 (copy enclosed) wherein Claim 8 is amended to place it in independent form and Claim 10 is amended to place it in independent form.

29 JUN 2004

The Examiner in his Response to Rule 312 Communication (PTO-271 (Rev. 04-01)) (copy enclosed) indicated on page 2 that:

"☒ 1. The amendment filed on 1/2/02 under 37 CFR 1.312 has been considered, and has been . . .

b). ☒ entered as directed to matters of form not affecting the scope of the invention."

The subject U.S. Patent No. 6,395,767 issued with Claim 8 and Claim 10 each being dependent on Claim 1, and without including Claim 8 and Claim 10 each being in independent form.

It is respectfully submitted that the Patent Office erred in not including Claim 8 and Claim 10 in independent form since the Examiner had entered Applicants' Amendment Under 37 CFR 1.312 to matters not affecting scope of the invention. Changing Claims 8 and 10 from dependent claims to independent claims does not change the scope of either Claim 8 or Claim 10. Either way, independent Claims 8 and 10 only cover the compounds in dependent Claims 8 and 10.

Accordingly, it is respectfully requested that the attached Certificate of Correction be approved and be included as part of the subject U.S. Patent No. 6,395,767.

Inasmuch as that this error was incurred by the Office, no fee is believed to be due. If any fee not accounted for is due in connection herewith, please charge such fee to Deposit Account No. 19-3880 of the undersigned.

Please send the Certificate to the address associated with customer account number 23914.

Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336

Burton Rodney
Attorney for Applicants
Reg. No. 22,076

Date: June 22, 2004

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Burton Rodney		Nov. 14, 2001
Type or print name	Signature	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

"B11

IN RE APPLICATION OF

ROBL ET AL.

APPLICATION NO: 09/788,173

FILED: FEBRUARY 16, 2001

FOR: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

Art Unit: 1626

Examiner: R. Gerstl

Assistant Commissioner for Patents
Box Issue Fee
Washington, D.C. 20231

AMENDMENT UNDER 37 CFR 1.312

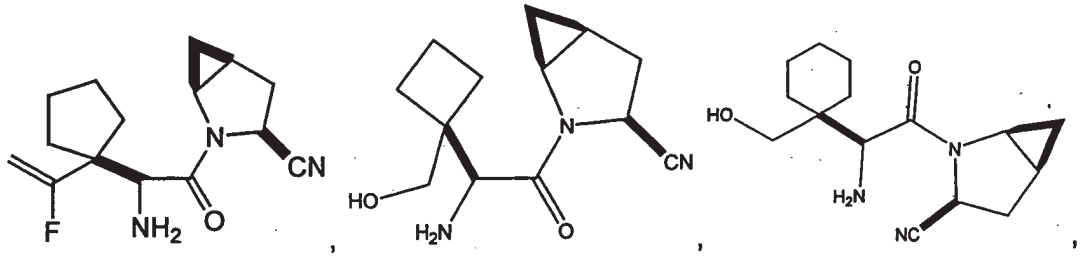
Sir:

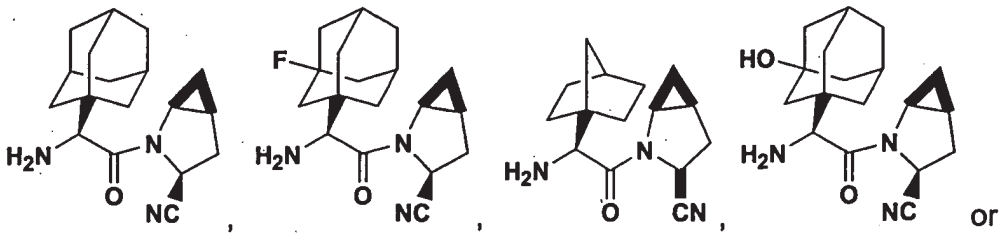
Please amend the above-identified application to read as follows:

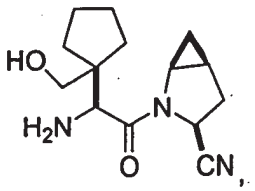
In the Claims:

Please amend Claims 8 and 10 to read as follows:

8. (Amended) A compound having the structure:

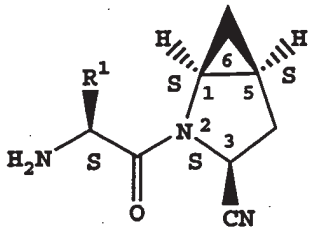






or a pharmaceutically acceptable salt thereof.

10. (Amended) A compound which is

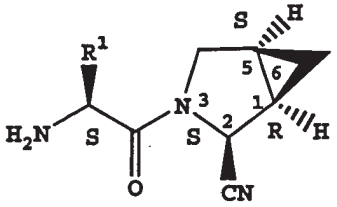


A

(1S,2(2S),3S,5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R,2S,3(2S),5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl.

Remarks

Claims 1 to 24 are present and have been allowed in the Notice of Allowance mailed October 19, 2001.

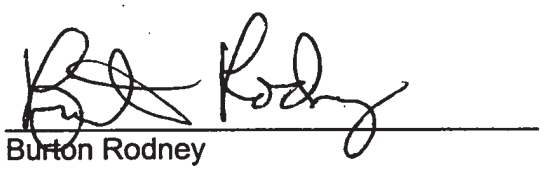
As seen above, Claims 8 and 10 have been amended to place each in independent form. No new matter has been added.

It is respectfully requested that the above amendments be entered.

A copy of Claims 8 and 10 with markings to show changes made is attached.

It is believed that this application is now in condition for issuance once the final fee has been paid.

Respectfully submitted,



Burton Rodney
Attorney for Applicants
Reg. No. 22,076

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336

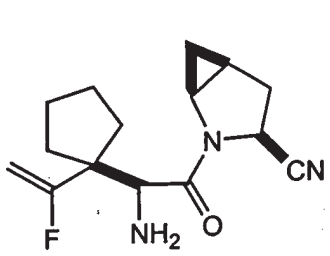
Date: Nov. 14, 2001

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 8 and 10 have been amended as follows:

-- 8. (Amended) [The] A compound [as defined in Claim 1] having the structure:



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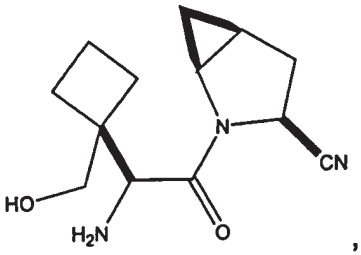

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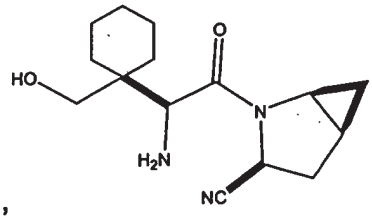

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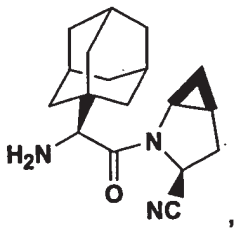

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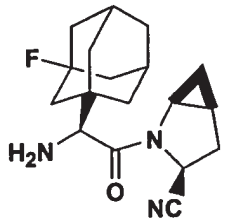

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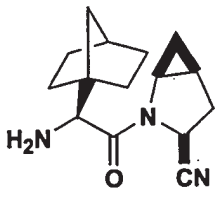
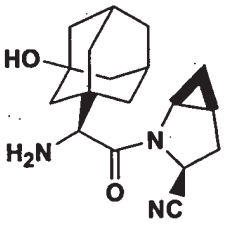
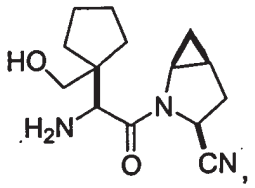


,


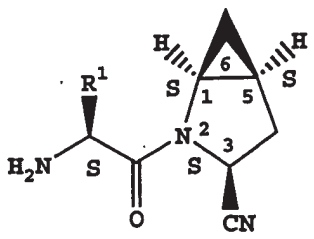
or



,

or a pharmaceutically acceptable salt thereof.--

--10. (Amended) [The] A compound [as defined in Claim 1] which is



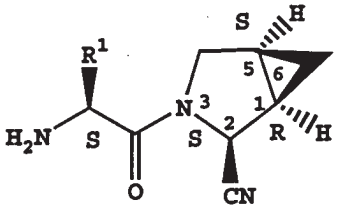
A

(1S,2(2S),3S,5S)

 0342

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R,2S,3(2S),5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl. --

Response to Rule 312 Communication	Application No.	Applicant(s)	
	09/788,173	ROBL ET AL.	
	Examiner	Art Unit	
	Robert Gerstl	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

1. ☒ The amendment filed on *12/20/01* under 37 CFR 1.312 has been considered, and has been:

a) ☐ entered.

b) ☒ entered as directed to matters of form not affecting the scope of the invention.

c) ☐ disapproved because the amendment was filed after the payment of the issue fee.
Any amendment filed after the date the issue fee is paid must be accompanied by a petition under 37 CFR 1.313(c)(1) and the required fee to withdraw the application from issue.

d) ☐ disapproved. See explanation below.

e) ☐ entered in part. See explanation below.

Robert Gerstl
Primary Examiner 29 JUN 2004
Art Unit: 1626

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Burton Rodney		9 - 12 - 05
Type or print name	Signature	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

ROBL ET AL

PATENT NO: 6,395,767

ISSUED: May 28, 2002

FOR: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
ATTENTION: Decision and Certificate of Correction
Branch of Patent Issue Division

REQUEST FOR SECOND CERTIFICATE OF CORRECTION FOR U.S. PATENT NO. 6,395,767 FOR PTO MISTAKE (37 C.F.R. §1.322(a))

Sir:

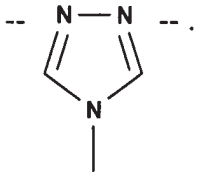
Attached, in duplicate, is PTO/SB/44 (also Form PTO-1050), with at least one copy being suitable for printing.

The exact page and line number where the errors are shown correctly in the application file Serial No. 09/788,173 (which issued into U.S. Patent No. 6,395,767) are as follows:

CORRECTION IN U.S. PATENT NO. 6,395,767 (basis in application)

In the Specification:

Col. 7, line 6, change "PGI" to -- PG_1 --. (page 9, line 37)

Col. 14, line 50, insert --  -- . (page 18, line 14, third formula)

Col. 14, line 56, between "refers" and "cycloheteroalkyl", insert -- to --. (page 18, line 17)

Col. 14, line 57, between "a" and "atom", insert -- C --. (page 18, line 19)

Col. 15, line 54, change "γ" to -- β --. (page 20, line 22)

Col. 20, line 59, "2,1" should be -- 2,3 --. (page 30, line 1)

Col. 29, line 23, change "w" to -- % --. (page 44, line 20)

Col. 30, line 2, after "$(M+H)^+$" and before "197", insert -- - --. (page 45, line 11)

Col. 32, line 62, after "$(M+H)^+$" and before "222", insert -- = --. (page 48, line 21)

Col. 33, line 3, change "HO" to read -- H_2O --. (page 48, line 29)

Col. 33, line 7, change "CH2cl$_2$" to read -- CH_2Cl_2 --. (page 49, line 2)

Col. 33, line 11, after "METHOD", insert -- A --. (page 49, line 6)

Col. 34, line 62, delete "15". (page 51, line 14)

Col. 41, line 43, after "was", delete "a". (page 60, line 12)

Col. 41, line 44, after "over", delete "a". (page 60, line 13)

Col. 43, line 36, delete "E". (page 63, line 18)

Col. 43, line 55, change "48.61" to -- 8.61 --. (page 63, line 31)

Col. 44, line 39, change "200" to -- 300 --. (page 65, line 5)

Col. 46, line 58, change "ter" to -- water --. (page 68, line 2)

Col. 46, line 58, after "20" and before "Detection", insert -- mL/min. --. (page 68, line 3)

Col. 46, line 65, change "dimethylcylopentanone" to -- dimethylcyclopentanone --. (page 68, line 9)

Col. 52, line 64, change "25" to -- 28 --. (page 75, line 17)

Col. 53, line 31, change "OSO_4" to -- OsO4 --. (page 76, line 8)

Col. 53, line 65, after "100%" and before "Solvent A", insert -- B, --. (page 77, line 6)

Col. 53, line 66, after "vent B =" and before "MeOH", insert -- 90% --. (page 77, line 7)

Col. 62, line 67, change "549" to -- 540 --. (page 90, line 3)

Col. 66, line 24, change "CH2Cl$_2$" to -- CH_2Cl_2 --. (page 94, line 20)

Col. 69, line 21, change "9" to -- 8 --. (page 98, line 18)

Col. 69, line 30, change "Hbl" to -- HCl --. (page 98, line 28)

Col. 70, line 56, move "Step 1" to line 65. (page 101, line 10)

Col. 72, line 36, change "50°" to -- 5° --. (page 103, line 22)

Col. 72, line 65, change "2.2(" to -- 2.28 --. (page 104, line 11)

Col. 72, line 65, change "30mL2" to --30 mL --. (page 104, line 11)

Col. 73, line 25, change "the n" to -- then --. (page 104, line 29)

Col. 73, line 26, change "et her" to -- ether --. (page 104, line 30)

Col. 74, line 32, change "50°" to -- 5° --. (page 106, line 10)

Col. 79, line 61, change "100" to -- 10% --. (page 113, line 23)

Col. 82, line 65, change "10EtOAc" to -- 10% EtOAc --. (page 118, line 4)

Col. 84, line 34, change "NS" to -- MS --. (page 120, line 17)

In the Claims:

Col. 92, line 42 (Claim 15), change "APR" to -- AR --. (page 132, line 17)

The above corrections are necessary because of errors by the PTO.

Accordingly, it is respectfully requested that the attached Certificate of Correction be approved and be included as part of the subject U.S. Patent No. 6,395,767.

Inasmuch as the errors necessitating the Certificate of Correction were incurred by the Office, no fee is believed to be due. If any fee not accounted for is due in connection herewith, please charge such fee to Deposit Account No. 19-3880 of the undersigned.

Please send the Certificate to the address associated with customer account number 23914.

Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336

Burton Rodney
Attorney for Applicant
Reg. No. 22,076

Date: 9-12-05

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

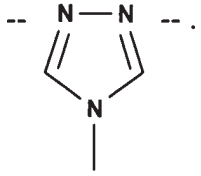
PATENT NO : 6,395,767
DATED: : May 28, 2002
INVENTOR(S) : Jeffrey A. Robl et al.

It is certified that there is an error in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Specification:

Col. 7, line 6, change "PGI" to -- PG_I --.

Col. 14, line 50, insert



Col. 14, line 56, between "refers" and "cycloheteroalkyl", insert -- to --.

Col. 14, line 57, between "a" and "atom", insert -- C --.

Col. 15, line 54, change "γ" to -- β --.

Col. 20, line 59, "2,1" should be -- 2,3 --.

Col. 29, line 23, change "w" to -- % --.

Col. 30, line 2, after "$(M+H)^+$" and before "197", insert -- - --.

Col. 32, line 62, after "$(M+H)^+$" and before "222", insert -- = --.

Col. 33, line 3, change "HO" to read -- H_2O --.

Col. 33, line 7, change "$CH2cl_2$" to read -- CH_2Cl_2 --.

Col. 33, line 11, after "METHOD", insert -- A --.

Col. 34, line 62, delete "15".

Col. 41, line 43, after "was", delete "a".

Col. 41, line 44, after "over", delete "a".

Col. 43, line 36, delete "E".

Col. 43, line 55, change "48.61" to -- 8.61 --.

Col. 44, line 39, change "200" to -- 300 --.

Col. 46, line 58, change "ter" to -- water --.

Col. 46, line 58, after "20" and before "Detection", insert -- mL/min. --.

Col. 46, line 65, change "dimethylcylopentanone" to -- dimethylcyclopentanone --.

Col. 52, line 64, change "25" to -- 28 --.

Col. 53, line 31, change "OSO_4" to -- OsO4 --.

Col. 53, line 65, after "100%" and before "Solvent A", insert -- B, --.

Col. 53, line 66, after "vent B =" and before "MeOH", insert -- 90% --.

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO : 6,395,767
DATED: : May 28, 2002
INVENTOR(S) : Jeffrey A. Robl et al.

It is certified that there is an error in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Col. 62, line 67, change "549" to -- 540 --.
Col. 66, line 24, change "CH2Cl$_2$" to -- CH_2Cl_2 --.
Col. 69, line 21, change "9" to -- 8 --.
Col. 69, line 30, change "Hbl" to -- HCl --.
Col. 70, line 56, move "Step 1" to line 65.
Col. 72, line 36, change "50°" to -- 5° --.
Col. 72, line 65, change "2.2(" to -- 2.28 --.
Col. 72, line 65, change "30mL2" to --30 mL --.
Col. 73, line 25, change "the n" to -- then --.
Col. 73, line 26, change "et her" to -- ether --.
Col. 74, line 32, change "50°" to -- 5° --.
Col. 79, line 61, change "100" to -- 10% --.
Col. 82, line 65, change "10EtOAc" to -- 10% EtOAc --.
Col. 84, line 34, change "NS" to -- MS --.

In the Claims:
Col. 92, line 42 (Claim 15), change "APR" to -- AR --.

MAILING ADDRESS OF SENDER:
Burton Rodney
Bristol-Myers Squibb Company
Patent Department
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PATENT NO. 6,395,767

SEP 2 6 2005

FORM PTO-1050

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,395,767 B2
DATED : May 28, 2002
INVENTOR(S) : Jeffrey A. Robl et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 7,
Line 6, change "PGI" to -- PG_1 --.

Column 14,
Line 50, insert --  --.

Line 56, between "refers" and "cycloheteroakyl", insert -- to --.
Line 57, between "a" and "atom", insert -- C --.

Column 15,
Line 54, change "γ" to -- β --.

Column 20,
Line 59, "2,1" should be -- 2,3 --.

Column 29,
Line 23, change "w" to -- % --.

Column 30,
Line 2, after "$(M+H)^+$" and before "197", insert -- - --.

Column 32,
Line 62, after "$(M+H)^+$" and before "222", insert -- = --.

Column 33,
Line 3, change "HO" to read -- H_2O --.
Line 7, change "$CH2cl_2$" to read -- CH_2Cl_2 --.
Line 11, after "METHOD", insert -- A --.

Column 34,
Line 62, delete "15".

Column 41,
Line 43, after "was", delete "a".
Line 44, after "over", delete "a".

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,395,767 B2
DATED : May 28, 2002
INVENTOR(S) : Jeffrey A. Robl et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 43,
Line 36, delete "E".
Line 55, change "48.61" to -- 8.61 --.

Column 44,
Line 39, change "200" to -- 300 --.

Column 46,
Line 58, change "ter" to -- water --.
Line 58, after "20" and before "Detection", insert -- mL/min. --.
Line 65, change "dimethylcylopentanone" to -- dimethylcyclopentanone --.

Column 52,
Line 64, change "25" to -- 28 --.

Column 53,
Line 31, change "OSO_4" to -- OsO4 --.
Line 65, after "100%" and before "Solvent A", insert -- B, --.
Line 66, after "vent B =" and before "MeOH", insert -- 90% --.

Column 62,
Line 67, change "549" to -- 540 --.

Column 66,
Line 24, change "$CH2Cl_2$" to read -- CH_2Cl_2 --.

Column 69,
Line 21, change "9" to -- 8 --.
Line 30, change "Hbl" to -- HCl --.

Column 70,
Line 56, move "Step 1" to line 65.

Column 72,
Line 36, change "50°" to -- 5° --.
Line 65, change "2.2(" to -- 2.28 --.
Line 65, change "30mL2" to -- 30 mL --.

Column 73,
Line 25, change "the n" to -- then --.
Line 26, change "et her" to -- ether --.

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,395,767 B2
DATED : May 28, 2002
INVENTOR(S) : Jeffrey A. Robl et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 74,
Line 32, change "50°" to -- 5° --.

Column 79,
Line 61, change "100" to -- 10% --.

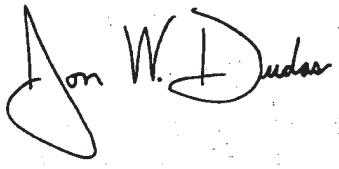
Column 82,
Line 65, change "10EtOAc" to -- 10% EtOAc --.

Column 84,
Line 34, change "NS" to -- MS --.

Column 92,
Line 42, change "APR" to -- AR --.

Signed and Sealed this

Twenty-ninth Day of November, 2005



JON W. DUDAS
Director of the United States Patent and Trademark Office

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

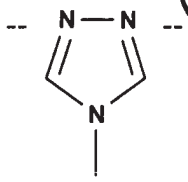
PATENT NO : 6,395,767 B1
DATED: May 28, 2002
INVENTOR(S) : Jeffrey A. Robl et al.

It is certified that there is an error in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

~~In the Specification:~~

Col. 7, line 6, change "PGI" to -- PG_1 --.

Col. 14, line 50, insert



Col. 14, line 56, between "refers" and "cycloheteroalkyl", insert -- to --.
Col. 14, line 57, between "a" and "atom", insert -- C --.
Col. 15, line 54, change "γ" to -- β --.
Col. 20, line 59, "2,1" should be -- 2,3 --.
Col. 29, line 23, change "w" to -- % --.
Col. 30, line 2, after "$(M+H)^+$" and before "197", insert -- - --.
Col. 32, line 62, after "$(M+H)^+$" and before "222", insert -- = --.
Col. 33, line 3, change "HO" to read -- H_2O --.
Col. 33, line 7, change "CH2cl2" to read -- CH_2Cl_2 --.
Col. 33, line 11, after "METHOD", insert -- A --.
Col. 34, line 62, delete "15".
Col. 41, line 43, after "was", delete "a".
Col. 41, line 44, after "over", delete "a".
Col. 43, line 36, delete "E".
Col. 43, line 55, change "48.61" to -- 8.61 --.
Col. 44, line 39, change "200" to -- 300 --.
Col. 46, line 58, change "ter" to -- water --.
Col. 46, line 58, after "20" and before "Detection", insert -- mL/min. --.
Col. 46, line 65, change "dimethylcylopentanone" to -- dimethylcyclopentanone --.
Col. 52, line 64, change "25" to -- 28 --.
Col. 53, line 31, change "OSO_4" to -- OsO4 --.
Col. 53, line 65, after "100%" and before "Solvent A", insert -- B, --.
Col. 53, line 66, after "vent B =" and before "MeOH", insert -- 90% --.

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO : 6,395,767 B2
DATED: : May 28, 2002
INVENTOR(S) : Jeffrey A. Robl et al.

It is certified that there is an error in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Col. 62, line 67, change "549" to -- 540 --.
Col. 66, line 24, change "CH2Cl$_2$" to -- CH_2Cl_2 --.
Col. 69, line 21, change "9" to -- 8 --.
Col. 69, line 30, change "Hbl" to -- HCl --.
Col. 70, line 56, move "Step 1" to line 65.
Col. 72, line 36, change "50°" to -- 5° --.
Col. 72, line 65, change "2.2(" to -- 2.28 --.
Col. 72, line 65, change "30mL2" to --30 mL --.
Col. 73, line 25, change "the n" to -- then --.
Col. 73, line 26, change "et her" to -- ether --.
Col. 74, line 32, change "50°" to -- 5° --.
Col. 79, line 61, change "100" to -- 10% --.
Col. 82, line 65, change "10EtOAc" to -- 10% EtOAc --.
Col. 84, line 34, change "NS" to -- MS --.

In the Claims:
Col. 92, line 42 (Claim 15), change "APR" to -- AR --.

MAILING ADDRESS OF SENDER:
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PATENT NO. 6,395,767

SEP 2 6 2005

FORM PTO-1050

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,395,767 B2
DATED : May 28, 2002
INVENTOR(S) : Jeffrey A. Robl et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 91,
Lines 9-10, should read -- A compound having the structure: --
Line 54, should read -- A compound which is --.

Issued

Signed and Sealed this

Twenty-seventh Day of July, 2004

Jon W. Dudas

JON W. DUDAS
Acting Director of the United States Patent and Trademark Office

Case: LA0050 NP

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO : 6,395,767 B2
DATED: : May 28, 2002
INVENTOR(S) : Jeffrey A. Robl, Richard B. Sulsky, David J. Augeri, David R. Magnin, David A. Betebenner

It is certified that there is an error in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims:

Claim 8, line 1 should read --A compound having the structure:--.

Claim 10, line 1 should read --A compound which is--.

Issued

MAILING ADDRESS OF SENDER:
Burton Rodney
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PATENT NO. 6,395,767

FORM PTO-1050

29 JUN 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(MBHB Case No. 07-1293)

U.S. Patent No.:	**6,395,767**	)
		)
Granted:	**May 28, 2002**	)
		)
Inventors:	**Robl *et al.***	)
		)
Serial No.:	**09/788,173**	)
		)
Filed:	**February 6, 2001**	)
		)
For:	**Cyclopropyl-fused Pyrrolidine-based Inhibitors of Dipeptidyl Peptidase IV and Method**	)

TRANSMITTAL LETTER

Mail Stop Hatch-Waxman PTE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22303-1450

Dear Sir:

In regard to the above-identified patent application:

1. We are transmitting herewith the attached:
   a. Request for Patent Term Extension and Exhibits (1 Original and two copies)
   b. Postcard
2. With respect to additional fees:
   ____ A. No additional fee is required.
   X B. Attached is a check in the amount of $1,120.00.
3. Please charge any additional fees or credit over-payments to the Deposit Account No.13-2490.
4. x The undersigned hereby certifies that this Transmittal Letter and this paper, as described in paragraph 1 hereinabove, are being hand-delivered, in an envelope addressed to: Office of Patent Legal Administration, Room MDW 7D55, 600 Dulany Street (Madison Building), Alexandria, VA 22314 on September 22, 2009.

Dated: September 21, 2009

By: _____
Kevin E. Noonan
Reg. No. 46,375

McDonnell Boehnen Hulbert & Berghoff, LLP
300 South Wacker Drive
Chicago, Illinois 60606
Tel: (312)913-0001

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(MBHB Case No. 07-1293)

U.S. Patent No.:	**6,395,767**	)
		)
Granted:	**May 28, 2002**	)
		)
Inventors:	**Robl *et al.***	)
		)
Serial No.:	**09/788,173**	)
		)
Filed:	**February 6, 2001**	)
		)
For:	**Cyclopropyl-fused Pyrrolidine-based Inhibitors of Dipeptidyl Peptidase IV and Method**	)

APPLICATION FOR PATENT TERM EXTENSION PURSUANT TO 35 U.S.C. §156

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22303-1450

Dear Sir:

Applicant, Bristol-Myers Squibb Company, the owner of record of U.S. Patent No. 6,395,767 ("the '767 patent"; *attached hereto* as Exhibit A) submits this Application for Patent Term Extension pursuant to the provisions of 35 U.S.C. §156. In making this application for patent term extension, Applicant has received regulatory approval of a new human anti-diabetic drug as disclosed below and claimed in the '767 patent.

I. Eligibility

Applicant is entitled to patent term extension for this patent on the grounds that

the circumstances fulfill the requirements of 35 U.S.C. §156. Specifically:

a) U.S. Patent 6,395,767 claims a product according to the provisions of §156(a);

b) The term of this patent has not expired before submission of this application for patent term extension pursuant to §156(a)(1);

c) The term of this patent has never been extended, pursuant to §156(a)(2);

d) Applicant is the owner of record of the patent according to the assignment documents appended to this application, pursuant to §156(a)(3);

e) The product has been subject to a regulatory review period before commercial marketing and use pursuant to §156(a)(4); and

f) Permission for commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provisions of the law under which the regulatory review period was conducted pursuant to §156(a)(5).

Applicant, Bristol-Myers Squibb Company, is the owner of all right, title and interest in U.S. Patent 6,395,767, as recorded by assignment in the U.S. Patent and Trademark Office at reel 11607 and frame 0369 (attached hereto as **Exhibit B**).

Bristol-Myers Squibb Company received regulatory approval for the approved product on July 31, 2009.

The term of U.S. Patent No. 6,395,767 has not expired prior to submission of this application.

II. Requirements

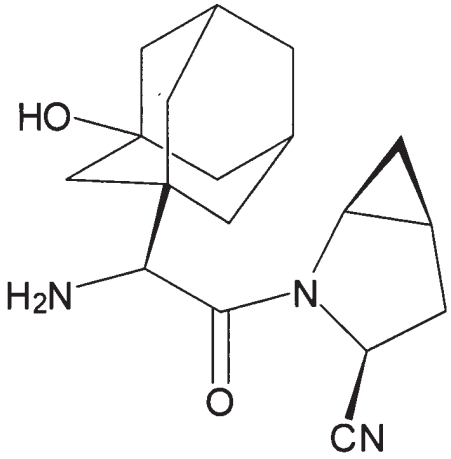
Applicant provides the following information, pursuant to the requirements of 35 U.S.C. §156(d) and 37 C.F.R. 1.740 *et seq.*:

(a) An application for extension of patent term must be made in writing to the Commissioner. A formal application for the extension of patent term must include:

(1) A complete identification of the approved product as by appropriate chemical and generic name, physical structure or characteristics;

The approved product is ONGLYZA® (generic name: saxagliptin), an anti-diabetic drug having the chemical name (1S,3S,5S)-2-[(2S)-amino(3-hydroxytricyclo[3.3.1.$1^{3,7}$]dec-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile.

This compound has the structural formula:



(2) A complete identification of the Federal statute including the applicable provision of law under which the regulatory review occurred;

The approved product was subject to regulatory review pursuant to 21 U.S.C. §355(a) and Title 505(b)(1) of the Federal Food, Drug and Cosmetic Act, *codified at* 21 U.S.C. §355(b)(1).

(3) An identification of the date on which the product received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred;

The product received permission for commercial marketing or use on July 31, 2009, pursuant to NDA 22-350 by the letter of that date from Curtis J. Rosebraugh, M.D.,

M.P.H., Director, Office of Drug Evaluation II, Center for Drug Evaluation and Research, Food and Drug Administration, Public Health Services, Department of Health and Human Services (attached hereto as **Exhibit C**).

(4) In the case of a drug product, an identification of each active ingredient in the product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act, or a statement of when the active ingredient was approved for commercial marketing or use (either alone or in combination with other active ingredients), the use for which it was approved, and the provision of law under which it was approved.

The active ingredient of the approved drug product is (1S,3S,5S)-2-[(2S)-amino(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile, generic name saxagliptin This active ingredient has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act.

The product has been approved as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

The product has been approved pursuant to 21 U.S.C. §355(a) and Title 505(b)(1) of the Federal Food, Drug and Cosmetic Act, *codified at* 21 U.S.C. §355(b)(1).

(5) A statement that the application is being submitted within the sixty day period permitted for submission pursuant to 37 C.F.R. § l.720(f) and an identification of the date of the last day on which the application could be submitted;

This application is submitted within 60 days of the date that the product first received permission for commercial marketing or use under the provisions of law under which the regulatory review period occurred, the last day for such submission being

September 28, 2009.

(6) A complete identification of the patent for which an extension is being sought by the name of the inventor, the patent number, the date of issue, and the date of expiration;

This application is made for U.S. Patent No. 6,395,767, issued May 28, 2002 to Jeffrey A. Robl, Richard B. Sulsky, David J. Augeri, David R. Magnin, Lawrence G. Hamann, and David A. Betebenner, and will expire on February 16, 2021.

(7) A copy of the patent for which an extension is being sought, including the entire specification (including claims) and drawings;

A copy of this patent is attached hereto as **Exhibit A**.

(8) A copy of any disclaimer, certificate of correction, receipt of maintenance fee payment, or reexamination certificate issued in the patent;

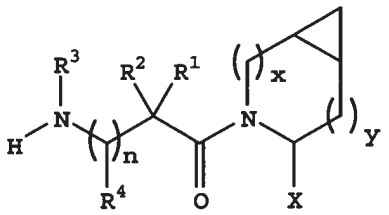
A copy of a receipt for payment of the first maintenance fee, paid November 4, 2005, is attached hereto as **Exhibit D**.

A copy of Certificates of Correction, filed July 27, 2004 and November 29, 2005 are attached hereto as **Exhibit E**.

(9) A statement that the patent claims the approved product, or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which at least one such patent claim reads on:

This patent claims the approved product and methods for using the approved product. Specifically, the approved product and methods for using the approved product are claimed in the following claims of U.S. Patent No. 6,395,767:

Claim 1. A compound having the structure



wherein x is 0 or 1 and y is 0 or 1, provided that

x = 1 when y = 0 and

x = 0 when y = 1; and wherein

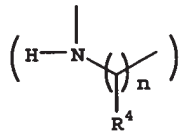
n is 0 or 1;

X is H or CN;

R^1, R^2, R^3 and R^4 are the same or different and are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl, hydroxybicycloalkyl, hydroxytricycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl; all optionally substituted through available carbon atoms with 1, 2, 3, 4 or 5 groups selected from hydrogen, halo, alkyl, polyhaloalkyl, alkoxy, haloalkoxy, polyhaloalkoxy, alkoxycarbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroarylamino, arylamino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro, cyano, amino, substituted amino, alkylamino, dialkylamino, thiol, alkylthio, alkylcarbonyl, acyl, alkoxycarbonyl, aminocarbonyl, alkynylaminocarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, alkylsulfonylamino, alkylaminocarbonylamino, alkoxycarbonylamino, alkylsulfonyl, aminosulfinyl, aminosulfonyl, alkylsulfinyl, sulfonamido or sulfonyl;

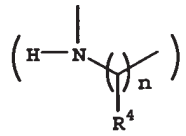
and R^1 and R^3 may optionally be taken together to form $-(CR^5R^6)_m-$ where m is 2 to 6, and R^5 and R^6 are the same or different and are independently selected from hydroxy, alkoxy, H, alkyl, alkenyl, alkynyl, cycloalkyl, halo, amino, substituted amino, cycloalkylalkyl, cycloalkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or R^1 and R^4 may optionally be taken together to form –

$(CR^7R^8)_p$- wherein p is 2 to 6, and R^7 and R^8 are the same or different and are independently selected from hydroxy, alkoxy, cyano, H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, halo, amino, substituted amino, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or optionally R^1 and R^3 together with



form a 5 to 7 membered ring containing a total of 2 to 4 heteroatoms selected from N, O, S, SO, or SO_2;

or optionally R^1 and R^3 together with



form a 4 to 8 membered cycloheteroalkyl ring wherein the cycloheteroalkyl ring has an optional aryl ring fused thereto or an optional 3 to 7 membered cycloalkyl ring fused thereto;

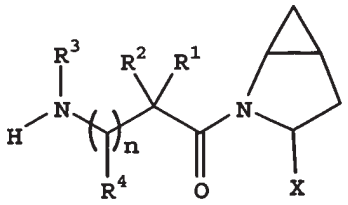
with the proviso that where x is 1 and y is 0, X is H, n is 0, and one of R^1 and R^2 is H and the other is alkyl, then R^3 is other than pyridyl or substituted pyridyl;

including all stereoisomers thereof;

and a pharmaceutically acceptable salt thereof, or a prodrug ester thereof, and all stereoisomers thereof.

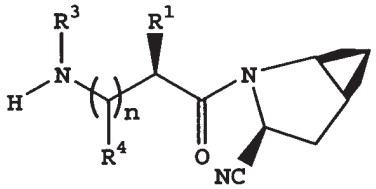
Claim 1 reads on the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 2. The compound as defined in claim 1 having the structure:



Claim 2 reads on the approved product when: n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 4. The compound as defined in claim 1 having the structure:



Claim 4 reads on the approved product when: n is 0; R^1 is hydroxytricycloalkyl; and R^3 is hydrogen.

Claim 6. The compound as defined in claim 1 wherein:

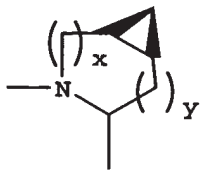
R^3 is H, R^1 is H, alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

R^2 is H or alkyl, n is 0,

X is CN.

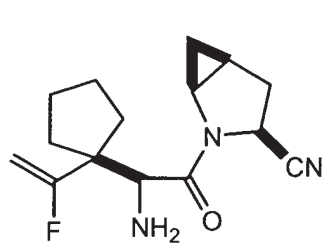
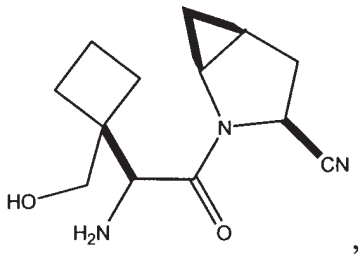
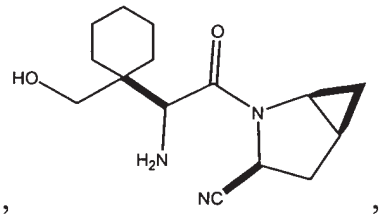
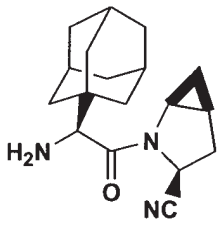
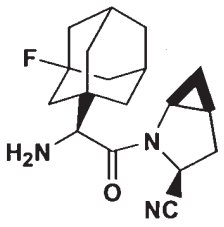
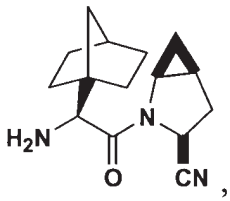
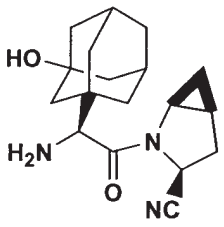
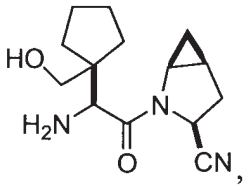
Claim 6 reads on the approved product when: x is 0; y is 1; R^1 is hydroxytricycloalkyl; and R^2 is H.

Claim 7. The compound as defined in claim 1 wherein the cyclopropyl fused to the pyrrolidine has the configuration:



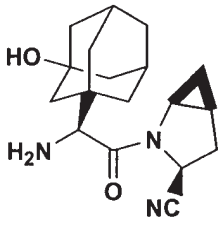
Claim 7 reads on the approved product when; x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 8. The compound as defined in claim 1 having the structure:

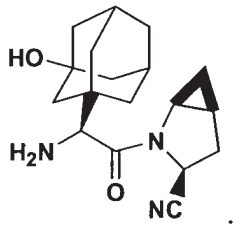
or a pharmaceutically acceptable salt thereof.

Claim 8 reads on the claimed product because it includes the structure

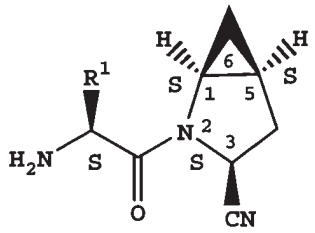


Claim 9. The compound as defined in claim 8 wherein the pharmaceutically acceptable salt is the hydrochloride salt or the trifluoroacetic acid salt.

Claim 9 reads on the approved product because it includes the structure



Claim 10. The compound as defined in claim 1 which is

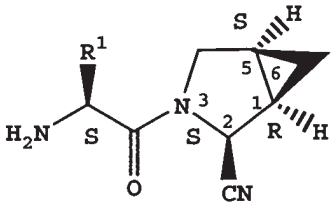


A

(1S,2(2S),3S,5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or

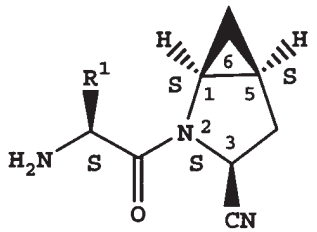


B

(1R,2S,3(2S),5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl.

Claim 10 reads on the approved product when the structure is



A

and R^1 is hydroxytricycloalkyl.

Claim 11. A pharmaceutical composition comprising a compound as defined in claim 1 and a pharmaceutically acceptable carrier therefor.

Claim 11 reads on a composition comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 12. A pharmaceutical combination comprising a DP4 inhibitor compound as defined in claim 1 and an antidiabetic agent other than a DP4 inhibitor for treating diabetes and related diseases, an anti-obesity agent and/or a lipid-modulating agent.

Claim 12 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 13. The pharmaceutical combination as defined in claim 12 comprising said DP4 inhibitor compound and an antidiabetic agent.

Claim 13 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 14. The combination as defined in claim 13 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR γ agonist, a PPAR α/γ dual agonist, an SGLT2 inhibitor, an aP2 inhibitor, a glycogen phosphorylase

inhibitor, an AGE inhibitor, an insulin sensitizer, a glucagon-like peptide-l (GLP-l) or mimetic thereof, insulin and/or a meglitinide.

Claim 14 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 15. The combination as defined in claim 14 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, Exendin-4, LY307161, NN2211, and/or LY315902.

Claim 15 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 16. The combination as defined in claim 13 wherein the compound is present in a weight ratio to the antidiabetic agent within the range from about 0.0l to about l00:l.

Claim 16 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 17. The combination as defined in claim 12 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor beta compound, an anorectic agent, and/or a fatty acid oxidation upregulator.

Claim 17 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 18. The combination as defined in claim 17 wherein the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, famoxin, and/or mazindol.

Claim 18 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 19. The combination as defined in claim 12 wherein the lipid modulating agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, an ACAT inhibitor, a cholesteryl ester transfer protein inhibitor, or an ATP citrate lyase inhibitor.

Claim 19 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 20. The combination as defined in claim 19 wherein the lipid modulating agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, nisvastatin, visastatin, fenofibrate, gemfibrozil, clofibrate, implitapide, CP-529,414, avasimibe, TS-962, MD-700, and/or LY295427.

Claim 20 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 21. The combination as defined in claim 19 wherein the DP4 inhibitor is present in a weight ratio to the lipid-modulating agent within the range from about 0.01 to about 100:1.

Claim 21 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 22. A pharmaceutical combination comprising a DP4 inhibitor compound as defined in claim 1 and an agent for treating infertility, an agent for treating polycystic ovary syndrome, an agent for treating a growth disorder and/or frailty, an anti-arthritis agent, an agent for preventing inhibiting allograft rejection in transplantation, an agent for treating autoimmune disease, an anti-AIDS agent, an agent for treating inflammatory bowel disease/syndrome, an agent for treating anorexia nervosa, an anti-osteoporosis agent and/or an anti-obesity agent.

Claim 22 reads on a combination comprising the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 23. A method for treating diabetes, insulin resistance, hyperglycemia, hyperisulinemia, or elevated blood levels of free fatty acids or glycerol, obesity, Syndrome X, dysmetabolic syndrome, diabetic complications, hypertriglyceridemia, hyperinsulinemia, atherosclerosis, impaired glucose homeostasis, impaired glucose tolerance, infertility, polycystic ovary syndrome, growth disorders, frailty, arthritis, allograft rejection in transplantation, autoimmune diseases, AIDS, intestinal diseases, inflammatory bowel syndrome, nervosa, osteoporosis, or an immunomodulatory disease or a chronic inflammatory bowel disease, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in claim 1.

Claim 23 reads on a method for using the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Claim 24. The method as defined in claim 23 for treating type II diabetes and/or obesity.

Claim 24 reads on a method for using the approved product when: x is 0; y is 1; n is 0; X is CN; R^1 is hydroxytricycloalkyl; and R^2 and R^3 are hydrogen.

Thus,

Claim 1 reads on the approved product.

Claim 2 reads on the approved product.

Claim 4 reads on the approved product.

Claim 6 reads on the approved product.

Claim 7 reads on the approved product.

Claim 8 reads on the approved product.

Claim 9 reads on the approved product.

Claim 10 reads on the approved product.

Claim 11 reads on the approved product.

Claim 12 reads on the approved product.

Claim 13 reads on the approved product.

Claim 14 reads on the approved product.

Claim 15 reads on the approved product.

Claim 16 reads on the approved product.

Claim 17 reads on the approved product.

Claim 18 reads on the approved product.

Claim 19 reads on the approved product.

Claim 20 reads on the approved product.

Claim 21 reads on the approved product.

Claim 22 reads on the approved product.

Claim 23 reads on a method for using the approved product.

Claim 24 reads on a method for using the approved product.

(10) A statement beginning on a new page of the relevant dates and information pursuant to 35 U.S.C. 156(g) in order to enable the Secretary of Health and Human Services or the Secretary of Agriculture, as appropriate, to determine the applicable regulatory review period as follows:

(i) For a patent claiming a human drug, antibiotic, or human biological product:

(A) The effective date of the investigational new drug (IND) application and the IND number;

(B) The date on which a new drug application (NDA) or a Product License Application (PLA) was initially submitted and the NDA or PLA number; and

(C) The date on which the NDA was approved or the Product License issued;

The following dates are relevant for a determination of the length of the Patent Term Extension available to applicant:

An Investigational New Drug (IND) application, No. 63,634 was filed November 8, 2001 (copy of FDA letter acknowledgment attached hereto as **Exhibit F**).

A New Drug Application (NDA), No. 22-350 was filed June 30, 2008 (copy of FDA letter acknowledgment attached hereto as **Exhibit G**).

An Approval letter for NDA No. 22-350 was signed July 31, 2009 (copy of FDA letter attached hereto as **Exhibit C**).

(11) A brief description beginning on a new page of the significant activities undertaken by the applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities;

Applicant submits its log of activities before the FDA as **Exhibit H**. The following provides a brief description of significant activities undertaken by the applicant during the regulatory review period with respect to the approved product, with significant dates:

- The original IND submission (IND 63,634) for ONGLYZA® (Saxagliptin) was submitted on **November 8, 2001**.

- Letter and telephonic correspondence between Applicant and FDA regarding protocol changes and ophthalmological data on **November 21, 2001**, **December 7, 2001**, **December 10, 2001** and **December 17, 2001**.

- In **2002**, protocol and information amendments submitted on **February 20**, **March 13**, **March 27**, and **November 12**; information submitted by Applicant on pharmacology/toxicology and safety on **March 4**, **June 7**, **August 9**, **November 18** and **December 18**; letter from FDA regarding clinical trials database on **April 11**.

- In **2003**, protocol and information amendments submitted on **January 31**, **March 26**, **April 21**, **June 3**, **June 25**, **July 17**, **July 31**, **August 6**, **August 26**, **September 15**, **September 30**, **October 7**, **October 9**, **October 30**, **November 17**, **December 2**, **December 12**, and **December 23**; information submitted by Applicant on stability, safety and pharmacology/toxicology on **January 24**, **January 31**, **February 21**, **May 6**, **May 21**, **July 29**, **August 11**, **September 30**, and **December 18**; telephone, facsimile and e-mail communications between Applicant and FDA on **April 1**, **April 3**, **April 4**, **April 8**, **April 9**, **April 16**, **April 18**, **April 23**, **April 28**, **August 13**, **October 15** (multiple), **October 29**, and **November 10**; FDA letter to Applicant with comments and request regarding

preclinical pharmacology review of IND on **July 7**; FDA letter regarding FDA review of Applicant September 30th submission on **October 6th**; Applicant submitted an IND annual report for period December 1, 2001 through November 20, 2002 on **April 14**.

- In **2004**, protocol amendments submitted on **February 27**, **March 18**, **May 19**, **June 28**, **July 16**, **August 6**, **August 25**, **September 14**, and **September 23**; information submitted by Applicant on stability, safety and pharmacology/toxicology on **January 8**, **January 16, February 25**, and **June 15**; telephone, facsimile and e-mail communications between Applicant and FDA on **February 3**, and **October 22**; Applicant submitted response to FDA CAC review of rat and mouse carcinogenicity study on **January 29th**; Applicant submitted an initial safety report on **February 11**; IND annual report Applicant submitted an IND annual report for period December 1, 2002 through November 20, 2003 on **February 12**; Applicant submitted letters requesting Type B End of Phase 2 meeting on **August 26**, **September 13**, and **December 20**, with FDA responses on **September 22** and **December 29** and telephone communication regarding cancellation of End of Phase 2 meeting on **October 21** (multiple).

- In **2005**, protocol amendments submitted on **June 16**, **June 23**, **July 20**, **August 24**, **August 25**, **September 8**, **September 9**, **September 27**, **October 5**, **October 13**, **October 25**, **November 7**, **November 16**, **December 12**, **December 14**, **December 16**, and **December 19**; information submitted by Applicant on stability, safety and pharmacology/toxicology on **January 14**, **February 22**, **March 2**, **May 11**, **June 20**, **July 22**, **August 30**, **October 10**, **October 14**, **November 30**, **December 1**, and **December 7**, including a final study report on **July 8** and **October** 14, a response to request for additional analysis of nonclinical saxagliptin exposure on **July 19**, and background briefing package for End of Phase 2 meeting on **August 22**; telephone, facsimile and e-mail communications between Applicant and FDA on **April 28**, **May 13**, **May 17**, **July 19**, **July 26**, **August 1**, **August 29**, **September 27**, **October 13** (multiple), **October 18** (multiple), **December 28** and **December 29**; Applicant submitted an

IND annual report for period December 1, 2003 through November 20, 2003 on **February 7**.

- On **July 15, 2005**, Applicant submitted a request for End of Phase 2 meeting. FDA letters providing details for End of Phase 2 meeting scheduled for July 27th, on **May 19**, official minutes of End of Phase 2 meeting on **August 23**, and comments and recommendations for June 5, 2005 submission on **August 24**. Applicant submitted briefing book for End of Phase 2 meeting and response to request for desk copy of protocol on **June 27**, an IND amendment submitted to provide drug products information to support Phase III clinical studies on **April 21** and an IND safety report regarding expedited investigator brochure on **October 13**. On **December 14, 2005**, FDA issued a letter providing comments and recommendations upon completion of review of November 7th submission. Applicant submitted a request for FDA review and comment on draft protocol for combination of saxagliptin and metformin on **December 22**.

- In **2006**, protocol amendments submitted on **January 12, January 27, February 14, March 7, March 13, March 17, March 23, March 30, April 24, April 27, April 28, May 11, May 17, May 24, June 2, June 19, July 7, July 12, August 15, August 17, September 6, September 18, September 22, September 27, October 3, October 18, October 19, November 3, November 16**, and **December 8**; information submitted by Applicant on stability, safety and pharmacology/toxicology on **January 13, February 24, March 23, June 2, June 29, August 4, September 18, September 19, November 3, November 17**, and **December 8**; telephone, facsimile and e-mail communications between Applicant and FDA on **January 30, January 31, February 3, April 26**, and **November 13**; Applicant submitted an IND annual report for period December 1, 2004 through November 20, 2005 on **February 3**.

- FDA issued letter regarding completion of review of December 14, 2005 amendment on **January 19** and **January 30, 2006**. Applicant submitted e-mail

response to FDA inquiry regarding saxagliptin combination questions on **January 25**.

- On **February 1, 2006**, telephone contact with FDA to clarify Applicant 's interest on Dr. Misbin's (Clinical Reviewer) comments on Protocol 013 (TZD study), as well as Applicant's decision to accept Dr. El-Hage's suggestion regarding control group in the rat carcinogenicity study.

- On **February 3, 2006**, Applicant submitted results of 1 to 3-month Monkey Toxicity Study.

- On **February 13, 2006**, FDA issued a draft statement for ESR.

- On **February 15, 2006**, Applicant submitted an IND safety report.

- On **April 20, 2006**, FDA issued letter regarding saxagliptin Capsules and Amendment dated 01/12-05 (New Protocol CV181033: Pharmacokinetic Drug Interaction Study with Saxagliptin and Simvastatin in Healthy Subjects), completed review with comments and recommendations. On **April 28** and **May 17, 2006**, FDA issued letters denying Applicant's Request for a Teleconference to discuss Saxagliptin progress and written responses to questions included in meeting request.

- On **May 26, 2006** Applicant submitted Request for FDA Review and Comment regarding The Planned Core Statistical Analysis Plan (CSAP)(BMS Doc. #930014584 v1.0) for the short-term periods of the Phase # Clinical Superiority Studies, and requests FDA input on the following protocols CV181011, CV181013, and CV181014. On **June 9**, **June 30, September 13**, **September 14**, and **October 30, 2006**, Applicant submitted IND safety reports regarding Supraventricular tachycardia. Report No. 1332659 and Anemia).

- In **2007**, protocol amendments submitted on **January 5**, **January 12**, **January 19**, **March 1**, **March 13**, **April 5**, **May 3**, **May 8**, **June 7**, **June 11**, **June 15**, **July 2**, **August 14**, **August 30**, **October 1**, **October 3**, **November 15**, **November 16**,

and **November 27**; information submitted by Applicant on stability, safety and pharmacology/toxicology on **January 12**, **March 5**, **March 12**, **April 19**, **May 3**, **May 30**, **June 7**, **September 5**, **September 12**, **September 14**, **September 26**, **October 2**, **October 16**, **October 18**, **October 19**, **October 23**, **October 24**, **November 6**, **November 8**, **November 12**, **November 15**, **November 16**, **December 14**, **December 20**, and **December 21**; telephone, facsimile and e-mail communications between Applicant and FDA on **April 11**, **May 3**, **May 9** through **June 22** (multiple) regarding denial of Applicant request for meeting, and **June 12** through **June 19**, regarding Applicant submission of Monkey Comparator test result from EMEA; Applicant submitted an IND annual report for period December 1, 2005 through November 20, 2006 on **February 5**.

- On **January 24, 2007**, telephone request from FDA for a revisit target submission date with an explanation for the Saxagliptin NDA. FDA also requested that Applicant submit to the Docket a revised target date for NDA submission with an explanation for submission timing.

- On **March 7, 2007**, FDA issued a letter regarding data indicating that the administration of dipeptidyl peptidase-4 (DPP-4) inhibitors to monkeys results in dose and duration-dependent increases in necrotizing cutaneous lesions of the periphery, including the tail, digits, hands/feet, ears, nose, and scrotum.

- On **March 15, 2007**, FDA issued a letter regarding FDA approval for a Type C meeting with Applicant, to discuss the quality portion of the upcoming NDA, as part of the CMC pilot program, to which Applicant responded with a Briefing Document on **April 11** for a meeting scheduled for **April 26**. FDA provided letter with official minutes of meeting on **May 25**.

- On **April 19, 2007**, FDA issued a letter regarding the amendment dated **January 22, 2007** (serial #0011), containing proposed QTc evaluation plan. QTc Team has completed their review of submission and has comments and recommendations.

- On **June 5, 2007**, Applicant provided additional data request by FDA relating to IND.

- On **September 14, 2007**, Applicant submitted a request for type B Pre-NDA Meeting to discuss several issues related to the format and content of the saxagliptin NDA, proposing a meeting date of **November 12, 14 or 16, 2007**.

- On **September 28, 2007**, Applicant submitted a Response to Agency Comments, Request for Review and Comment. Applicant are now providing for the Agency's review and comment Protocol D1680C00007 CV181-062 dated 20-Sept-2007 (DCN 930023980 v2.0) and (DCN 930023982 v1.0).

- On **October 15, 2007**, Applicant submitted a Pre-NDA Briefing Document as requested by the FDA, including a final agenda and set of questions that Applicant planned to discuss at the meeting.

- On **December 27, 2007**, Applicant submitted CMC-Correspondence to the IND in reference to minutes from April 26, 2007 meeting, included with this correspondence two CMC questions related to Applicant upcoming NDA for Saxagliptin tablets.

- In **2008**, protocol amendments submitted on **January 16**, **January 18**, **February 8**, **February 11**, **February 27**, **March 14**, **March19**, **June 5**, and **June 18**; information submitted by Applicant on stability, safety and pharmacology/toxicology on **January 8**, **January 17**, **February 14**, **February 25**, **March 6**, **March 11**, **March 27**, **April 23**, **April 25**, **April 30**, and **May 8**; telephone, facsimile and e-mail communications between Applicant and FDA on **April 11**; Applicant submitted an IND annual report for period December 1, 2006 through November 20, 2007 on **February 5**.

- On **January 8, 2008**, FDA issued a letter providing comments and recommendations on amendment submitted by Applicant on September 28, 2007, containing protocol d1680c00007.

- On **February 15, 2008**, Applicant submitted a Response to request for information regarding entire submission dated Oct 23, 2007; IB submitted on June 20, 2007; study rpt. for CV181001 submitted on Feb 22, 2005; study report for CV181002 submitted on Jul 8, 2005 and study report for CV181010 submitted on Oct 19, 2007.

- On **March 16, 2008**, FDA issued a letter regarding FDA's comments and request for a written response upon completion of FDA review of Applicant 's responses to FDA's comments in a letter dated Jan 3, 2008 with regards to Protocol D1680C00007. This is in reference to the amendment dated **Feb 29, 2008**.

- On **June 19, 2008**, Applicant provided a response to FDA request for information regarding the Agency's comment (no. 7), requesting a justification for the plan to submit results from the study (Protocol D1680C00007) after the planned action date of the saxagliptin NDA.

- On **June 30, 2008**, Applicant submitted a New Drug Application (NDA 22-350) for ONGLYZA® as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus to the United States Food and Drug Administration (FDA).

- On **August 28, 2008**, Applicant provided datasets for carcinogenicity studies DN03100 and DN05004 for saxagliptin.

- On **September 26, 2008**, Applicant resubmitted corrected datasets for CV 181-013 LT.

- On **October 15, 2008**, Applicant responded to CMC question in FDA letter dated September 12, 2008.
- On **October 24, 2008**, Applicant responded to FDA request for information dated September 12 2008 specifically questions 1, 3, 4, 6, 7, 8, 9 & 10.

- On **October 28, 2008**, Applicant provided 120-day safety update for saxagliptin, including clinical safety update on several clinical protocols.

- On **October 29, 2008**, Applicant provided case report forms in support of 120-day clinical safety update.

- On **November 3, 2008**, Applicant provided responses to clinical questions 2 and 5, biostatistics questions 11 and 12 and CMC questions 16(c) and 16(f) from FDA letter dated September 12, 2008.

- On **November 14, 2008**, Applicant provided final responses for all Serious Adverse Events for subjects in control groups for Clinical Question #3.

- On **November 19, 2008**, Applicant provided responses to Clinical Pharmacology request for data sets used for the population pK analysis (for both parent and metabolite) and exposure-response analysis with regard to HbA1c, plasma fasting glucose and lympholysis.

- On **November 24, 2008**, Applicant proposed pediatric study and request for partial pediatric waiver.

- On **December 2, 2008**, Applicant provided a response to FDA request for clinical pharmacology information.

- On **December 15, 2008**, Applicant provided a response to FDA request for additional information.

- On **December 16, 2008**, Applicant provided response to FDA CMC request.

- On **December 23, 2008**, Applicant provided response to FDA questions issued December 19, 2008, regarding clarification of potential statistical errors.

- On **December 24, 2008**, Applicant reviewed FDA request for additional information regarding "ST" and "UP TO WEEK 24" relating to clinical information requests dated **December 19, 2008** and provided additional long term stability study date during the review process.

- On **January 21, 2009**, Applicant provided a response to information request dated **January 11, 2009** and CMC request for information dated **December 1, 2008**.

- On **January 22, 2009**, Applicant provided response to FDA request for additional information contained in e-mail communication dated December 19, 2008.

- On **January 23, 2009**, Applicant provided a timeline for submission of responses to FDA request for clinical IR questions and provided response to FDA request for additional information.

- On **January 26, 2009**, Applicant provided response to FDA request for additional information and submitted final Clinical Study Report for CV181059.

- On **February 3, 2009**, Applicant provided response to FDA request for additional information contained in e-mail communication dated December 11, 2008.

- On **February 19, 2009**, Applicant provided corrections to response for information contained in FDA letter dated September 12, 2008, provided amended replacement response to clinical question 6 and provided response to FDA request for information dated January 28, 2009

- On **February 24, 2009**, Applicant provided response to FDA request for additional information contained in e-mail communication dated January 30, 2009.

- On **February 26, 2009**, FDA proposed new dates for FDA inspection in Canada, and Applicant provided response to FDA request for information in letter dated December 11, 2008.

- On **March 11, 2009**, Applicant provided responses to FDA's request for information regarding additional CMC information and to FDA request that dissolution testing be performed on every batch of saxagliptin tablets.

- On **March 16, 2009**, Applicant provided correction for handling localized edema Adverse Events.

- On **April 2, 2009**, Applicant provided response to FDA request for additional information contained in e-mail communication dated March 18, 2009.

- On **April 6, 2009**, Applicant provided response to request for information regarding location for laboratory shift tables for pooled monotherapy studies.

- On **April 15, 2009**, Applicant provided response to request for information regarding report of rat embryo-fetal development.

- On **April 20, 2009**, Applicant provided response to request for information providing tables to relevant literature and study report references in DN08072.

- On **April 23, 2009**, Applicant provided response to request for cardiovascular outcomes study design concept.

- On **May 19, 2009**, FDA and Applicant correspondence regarding request for change in timelines for cardiovascular outcomes study design concept.

- On **May 27, 2009**, Applicant submitted response to FDA request dated May 12, 2009 for information regarding analysis of pancreatitis cases after saxagliptin administration and comparators in controlled Phase II/III clinical trials.

- On **June 3, 2009**, Applicant submitted response to e-mail communication from FDA dated May 11, 2009 regarding requests for additional information relating suspension from Russia.

- On **June 17, 2009**, Applicant submitted response to FDA letter dated March 25, 2009 regarding requests for additional information and e-mail communication dated June 12, 2009.

- On **June 23, 2009**, Applicant provided response to request for additional information in e-mail communication from FDA dated June 4, 2009.

- On **July 6, 2009**, Applicant submitted response to FDA request for revised carton and container labels.

- On **July 17, 2009**, Applicant submitted responses to multiple FDA requests for information contained in e-mails dated June 26 and June 28, 2009.

- On **July 17, 2009**, Applicant submitted responses to FDA requests for additional label revisions for 5mg strength on physician sample pack.

- On **July 22, 2009**, Applicant submitted case report forms for 18 hypersensitivity cases, and responses to requests dated July 7 and 8, 2009 for incidence of fracture and renal analysis on 120-day safety update.

- On **July 22, 2009**, Applicant submitted response to FDA request dated July 10, 2009, providing narratives for cases of "Alt" and "Hy's Law" in clinical trials since DB lock for 120-day safety update.

- On **July 27, 2009**, Applicant submitted response to request for additional information regarding narratives for 18 hypersensitivity cases to determine whether reactions had signs and symptoms of anaphylaxis.

- On **July 28, 2009**, Applicant provided chemical name of saxagliptin major metabolite and simplified variation thereof.

- On **July 28, 2009**, Applicant submitted response to request for information providing 2-hr. postprandial glucose excursions for Phase III clinical trials.

- On **July 29, 2009**, Applicant submitted response to request for information providing 2-hr. postprandial glucose excursions for Phase III clinical trials.

- ONGLYZA® NDA 22-350 was approved by the FDA on **July 31, 2009** following multiple interactions with the Agency regarding the content of final product

(12) A statement beginning on a new page that in the opinion of the applicant the patent is eligible for the extension and a statement as to the length of extension claimed, including how the length of extension was determined;

Applicant submits that U.S. Patent No. 6,395,767 is entitled to patent term extension according to the provisions of 35 U.S.C. §156. Applicant believes that the length of the extension of the patent term is equal to 896 days, pursuant to the provisions of 35 U.S.C. §§156(c) and (g).

The length of the patent term extension requested in this application is 896 days, comprising half of the period from November 8, 2001 until June 30, 2008 (a total of 2,426/2 = 1,213 days) plus the period from June 30, 2008 until July 31, 2009 (396 days), for a total of 1,609 days, as limited by the proviso of 35 U.S.C. §156(g)(6) that the total patent term extension is limited to be no longer than five (5) years (1,825 days), and further limited by the proviso of 35 U.S.C. §156(c)(3) that the total patent term is limited to be no longer than fourteen (14) years from the date of marketing approval, calculated as follows:

Length of regulatory review period under IND:

November 8, 2001 - November 7, 2002	=	365 days
November 8, 2002 - November 7, 2003	=	365 days
November 8, 2003 - November 7, 2004	=	366 days
November 8, 2004 - November 7, 2005	=	365 days
November 8, 2005 - November 7, 2006	=	365 days
November 8, 2006 - November 7, 2007	=	365 days
November 8, 2007 - June 30, 2008	=	235 days
Total	=	2,426 days

Length of regulatory review under NDA:

June 30, 2008 - June 29, 2009	=	365 days
June 30, 2009 - July 31, 2009	=	32 days
Total	=	396 days

Length of time from current expiration date of U.S. Patent No. 6,395,767 and fourteen years from July 31, 2009:

February 16, 2021 - February 15, 2022	= 365 days
February 16, 2022 - February 15, 2023	= 365 days
February 15, 2023 - July 31, 2023	= 166 days
Total	= 896 days

Applicant is applying for a patent term extension to the fullest extent that the patent deserves under the circumstances of regulatory delay set forth herein. Applicant believes the length of the patent term extension determined above is the appropriate length pursuant to the statute. Despite Applicant's diligent efforts, if the total number of days to which U.S. Patent No. 6,395,767 is greater than the number of days (896) requested here, Applicant requests the U.S. Patent and Trademark Office recalculate the correct length of patent term extension and award a patent term extension to U.S. Patent No. 6,395,767 for the correct number of days.

(13) A statement that applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought;

Applicant and its undersigned agent acknowledges a duty to disclose to the Director of the U.S. Patent and Trademark Office and the Secretary of Health and Human Services any information that is material to the determination of entitlement to the patent term extension sought in this application.

(14) The prescribed fee for receiving and acting upon the application for extension pursuant to 37 C.F.R. § 120(j)

The prescribed fee of one thousand one hundred twenty dollars ($1,120.00) as set forth in 37 C.F.R. §1.20(j) accompanies this application. The U.S. Patent and

Trademark Office is authorized to charge Deposit Account 13-2490 for the full amount of any deficiency in this fee.

(15) The name, address, and telephone number of the person to whom inquiries and correspondence relating to the application for patent term extension are to be directed.

Inquiries and correspondence relating to this patent term extension application should be addressed to:

Kevin E. Noonan
McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, IL 60606
(312) 913-2145 (direct)
(312) 913-0002 (facsimile)
noonan@mbhb.com

A Power of Attorney from applicant and a Rule 3.73(b) document are appended hereto as **Exhibit I**.

If the Examiner or other Patent Office official reviewing this application believes it to be helpful, he or she is invited to contact the undersigned attorney by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Date: September 21, 2009

By: _____
Kevin E. Noonan
Reg. No. 35,303

LIST OF EXHIBITS

Exhibit A: U.S. Patent No. 6,395,767

Exhibit B: U.S. Patent and Trademark Office assignment record for U.S. Patent No. 6,395,767

Exhibit C: ONGLYZA® FDA approval letter

Exhibit D: Copy of a receipt for payment of the first maintenance fee, paid **November 4, 2005**

Exhibit E1: Copy of a Certificates of Correction, filed **July 27, 2004** and **November 29, 2005**

Exhibit F: FDA acknowledgement letter for filing an New Drug (IND) application, No. **63,634**

Exhibit G: FDA acknowledgment letter for filing a New Drug Application (NDA), No. 22-350

Exhibit H: FDA Log

Exhibit I: Power of Attorney and Rule 3.73(b) document