

PATENT COOPERATION TREATY

From the 237
INTERNATIONAL SEARCHING AUTHORITY

To: Merck & Co Inc
126 East Lincoln Ave
Rahway, NJ 07065-0907

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing (day/month/year)	24 SEP 2007
FOR FURTHER ACTION See paragraph 2 below	

Applicant's or agent's file reference
PCT 22125Y

International application No.
PCT/US 07/00183

International filing date (day/month/year)
08 January 2007 (08.01.2007)

Priority date (day/month/year)
12 January 2006 (12.01.2006)

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - A01N 43/00 (2007.01); A61K 31/33 (2007.01)
USPC - 514/183

Applicant **Merck & Co Inc**

1. This opinion contains indications relating to the following items:
- Box No. I Basis of the opinion
 - Box No. II Priority
 - Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - Box No. IV Lack of unity of invention
 - Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - Box No. VI Certain documents cited
 - Box No. VII Certain defects in the international application
 - Box No. VIII Certain observations on the international application
2. **FURTHER ACTION**
- If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.
- If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.
- For further options, see Form PCT/ISA/220.
3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Date of completion of this opinion 15 July 2007 (15.07.2007)	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - the international application in the language in which it was filed.
 - a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of:
 - a. type of material
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material
 - on paper
 - in electronic form
 - c. time of filing/furnishing
 - contained in the international application as filed
 - filed together with the international application in electronic form
 - furnished subsequently to this Authority for the purposes of search
4. In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-12	YES
	Claims	NONE	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-12	NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims	NONE	NO

2. Citations and explanations:

Claims 1-12 lack an inventive step under PCT Article 33(3) as being obvious over US 5,369,108 A to Breslow et al. (hereinafter 'Breslow').

As per claim 1, Breslow teaches a hydroxyalkylarylamide compound comprising an amino substituted phenyl-NH-C(O)-phenyl wherein R10 is H (col 5, ln 32), R2 is alkyl (col 5, ln 33) which includes methyl and ethyl, R1 is R5C(O)- (col 5, ln 28 such that Y is alkyl amino) linked to the backbone benzyl structure (col 21, ln 5-10) further wherein R2 is phenyl (col 21, on 5-10), R4 is L2-R8 such that L2 is a bond and R8 is heteroaryl (col 2, ln 60-63 in that R1 is a substituted arylamino), n is 0 (col 4, ln 7) and R3 is NH2 (col 19, ln 15). The particular compound discussed above includes both N-(2-amino-5-thiophen-2-yl-phenyl)-4-(1-hydroxy-1-methylcarbamoyl-ethyl)-benzamide of claim 9 and N-(2-amino-5-thiophen-2-yl-phenyl)-4-(1-hydroxyethyl)benzamide of claim 10. Although Breslow does not describe this set of moieties in one example, Breslow teaches the backbone and suggests each substituent and moiety group. Therefore, it would have been obvious to one of ordinary skill in the art to make and use the claimed compound.

As per claim 2, as in claim 1, Breslow teaches a hydroxyalkylarylamide compound comprising an amino substituted phenyl-NH-C(O)-phenyl wherein R10 is H (col 5, ln 32), R2 is alkyl (col 5, ln 33) which includes methyl and ethyl, R1 is R5C(O)- (col 5, ln 28 such that Y is alkyl amino) linked to the backbone benzyl structure (col 21, ln 5-10) further wherein R2 is phenyl (col 21, on 5-10), R4 is L2-R8 such that L2 is a bond and R8 is heteroaryl (col 2, ln 60-63 in that R1 is a substituted arylamino), n is 0 (col 4, ln 7) and R3 is NH2 (col 19, ln 15).

As per claim 3, as in claim 2, Breslow teaches a hydroxyalkylarylamide compound comprising an amino substituted phenyl-NH-C(O)-phenyl wherein R10 is H (col 5, ln 32), R2 is alkyl (col 5, ln 33) which includes methyl and ethyl, R1 is R5C(O)- (col 5, ln 28 such that Y is alkyl amino) linked to the backbone benzyl structure (col 21, ln 5-10) further wherein R2 is phenyl (col 21, on 5-10), R4 is L2-R8 such that L2 is a bond and R8 is heteroaryl (col 2, ln 60-63 in that R1 is a substituted arylamino), n is 0 (col 4, ln 7) and R3 is NH2 (col 19, ln 15).

As per claim 4, as in claim 1, Breslow teaches a hydroxyalkylarylamide compound wherein R1 is R5C(O)- (col 5, ln 28 such that Y is alkyl amino) linked to the backbone benzyl structure (col 21, ln 5-10) further wherein R2 is phenyl (col 21, on 5-10), R4 is L2-R8 such that L2 is a bond and R8 is heteroaryl (col 2, ln 60-63 in that R1 is a substituted arylamino), n is 0 (col 4, ln 7) and R3 is NH2 (col 19, ln 15).

As per claim 5, as in claim 2, Breslow teaches a hydroxyalkylarylamide compound wherein Ar is phenyl, R1 is R5C(O)- (col 5, ln 28 such that Y is alkyl amino) linked to the backbone benzyl structure (col 21, ln 5-10) further wherein R2 is phenyl (col 21, on 5-10), R4 is L2-R8 such that L2 is a bond and R8 is heteroaryl (col 2, ln 60-63 in that R1 is a substituted arylamino), n is 0 (col 4, ln 7) and R3 is NH2 (col 19, ln 15).

As per claim 6, as in claim 5, Breslow teaches a hydroxyalkylarylamide compound wherein R10 is H (col 5, ln 32), R2 is alkyl (col 5, ln 33) which includes methyl and ethyl, R1 is R5C(O)- (col 5, ln 28 such that Y is alkyl amino) linked to the backbone benzyl structure (col 21, ln 5-10) further wherein R2 is phenyl (col 21, on 5-10), R4 is L2-R8 such that L2 is a bond and R8 is heteroaryl (col 2, ln 60-63 in that R1 is a substituted arylamino), n is 0 (col 4, ln 7) and R3 is NH2 (col 19, ln 15).

As per claim 7, as in claim 2, Breslow teaches a hydroxyalkylarylamide compound comprising 5 membered heteroaryl group (col 23, ln 40-50) linked to -NH-C(O)-phenyl wherein R10 is H (col 5, ln 32), R2 is alkyl (col 5, ln 33) which includes methyl and ethyl, R1 is R5C(O)- (col 5, ln 28 such that Y is alkyl amino) linked to the backbone benzyl structure (col 21, ln 5-10) further wherein R2 is phenyl (col 21, on 5-10), R4 is L2-R8 such that L2 is a bond and R8 is heteroaryl (col 2, ln 60-63 in that R1 is a substituted arylamino), n is 0 (col 4, ln 7) and R3 is NH2 (col 19, ln 15). Although Breslow does not teach the specific heteroaryl group, it would have been obvious to one of ordinary skill in the art to modify the reference without undue experimentation since Breslow teaches 5 membered heteroaryl rings.

As per claim 8, as in claim 7, Breslow teaches a hydroxyalkylarylamide compound comprising 5 membered heteroaryl group (col 23, ln 40-50) linked to -NH-C(O)-phenyl wherein R10 is H (col 5, ln 32), R2 is alkyl (col 5, ln 33) which includes methyl and ethyl, R1 is R5C(O)- (col 5, ln 28 such that Y is alkyl amino) linked to the backbone benzyl structure (col 21, ln 5-10) further wherein R2 is phenyl (col 21, on 5-10), R4 is L2-R8 such that L2 is a bond and R8 is heteroaryl (col 2, ln 60-63 in that R1 is a substituted arylamino), n is 0 (col 4, ln 7) and R3 is NH2 (col 19, ln 15).

-----continued in Supplemental Box-----

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box V.2. Citations and explanations:

As per claims 9 and 10, Breslow teaches a hydroxyalkylarylamide compound as discussed in claim 1. In particular, Breslow teaches a compound comprising an amino substituted phenyl-NH-C(O)-phenyl wherein R10 is H (col 5, ln 32), R2 is alkyl (col 5, ln 33) which includes methyl and ethyl, R1 is R5C(O)- (col 5, ln 28 such that Y is alkyl amino) linked to the backbone benzyl structure (col 21, ln 5-10) further wherein R2 is phenyl (col 21, on 5-10), R4 is L2-R8 such that L2 is a bond and R8 is heteroaryl (col 2, ln 60-63 in that R1 is a substituted arylamino), n is 0 (col 4, ln 7) and R3 is NH2 (col 19, ln 15). Put together as a whole, the variables discussed above teach both N-(2-amino-5-thiophen-2-yl-phenyl)-4-(1-hydroxy-1-methylcarbamoyl-ethyl)-benzamide of claim 9 and N-(2-amino-5-thiophen-2-yl-phenyl)-4-(1-hydroxyethyl)benzamide of claim 10.

As per claim 11, as in any of claims 1-10, Breslow teaches the compound comprising a pharmaceutical composition comprising a pharmaceutically acceptable carrier (Abstract).

As per claim 12, as in any of claims 1-10, Breslow teaches the compound for the preparation of a medicament useful in the treatment of cancer in a mammal (col 11, ln 53).

Claims 1-12 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.