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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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13/866,353

04/19/2013

Guoxian Wu

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99362

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10/04/2013

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EXAMINER

WANG, SHENGJUN

ART UNIT

PAPER NUMBER

1627

MAIL DATE

DELIVERY MODE

10/04/2013

PAPER

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

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 13/866,353	Applicant(s) WU ET AL.	
	Examiner SHENGJUN WANG	Art Unit 1627	AIA (First Inventor to File) Status No

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

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8/8/2013.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 1-20 is/are pending in the application.
5a) Of the above claim(s) 3,7,9-11,15,19 and 20 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 1,2,4-6,8,12-14 and 16-18 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

- 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)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 3) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>5/17/2013;7/18/2013</u> . | 4) <input type="checkbox"/> Other: ____. |

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

1. Claims 19-20 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, claims 3, 7, 9-11 and 15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 8, 2013.
2. The restriction requirement between groups I and II set forth in prior office action is withdrawn in view of applicants' traverse and the fact that pharmaceutical utility is the only disclosed utility of the compounds.
3. Applicant's election without traverse of inventions group I and II in the reply filed on August 8, 2013 is acknowledged. Applicants also elect compound species of formula Ic, wherein on R1 is CH₃ and the other R1 is pyrimidinyl; R2 is H; R3 is phenyl; R4 is H; and Ar is thiazolyl.
4. The claims have been examined insofar as they read on the elected invention and species.

PRIORITY

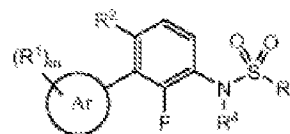
5. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or

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provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of 35 U.S.C. 112(a) or the first paragraph of pre-AIA 35 U.S.C. 112, except for the best mode requirement. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994)

The disclosure of the prior-filed application, Application No. 12/669,450, fails to provide adequate support or enablement in the manner provided by 35 U.S.C. 112(a) or pre-AIA 35 U.S.C. 112, first paragraph for one or more claims of this application. The claims herein require



particularly combination of the substituents on the core structure Formula 1c, which is lack support from the prior-filed application 12/669,450. '450 provides no guidance, direction or working examples to reach the particular combination herein. This is particularly true for the elected species, and the compound recited in claim 15 which have specific requirement of each and every substituents. Such compounds have nowhere to be found in '450.

6. Applicant states that this application is a continuation or divisional application of the prior-filed application. A continuation or divisional application cannot include new matter. Applicant is required to change the relationship (continuation or divisional application) to continuation-in-part because this application contains the following matter not disclosed in the prior-filed application: The claims herein.

Specification Objection

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7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The content of the claims should be incorporated into the specification.

Claim Rejections 35 U.S.C. 112

8. The following is a quotation of 35 U.S.C. 112(a):

(a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), first paragraph:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 2, 4-6, 8, 12-14, and 16-18 are rejected under 35 U.S.C. 112(a) or 35 U.S.C.

112 (pre-AIA), first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for pre-AIA the inventor(s), at the time the application was filed, had possession of the claimed invention. Particularly, the elected species lack support from the application as originally filed.

The most relevant disclosure to the elected species is claim 15, which differs from the elected species in that R1 is methyl and pyrimidinyl vs. t-butyl and pyrimidinyl substituted with NH₂; R3 is phenyl vs. phenyl substituted with two fluoro groups and Ar is thiazolyl vs. 4-thiazolyl.

The application provides no guidance or direction to make such differences. ***This is a new matter rejection.***

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10. Claims 1, 2, 4-6, 8, 12-14 and 16-18 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for pre-AIA the inventor(s), at the time the application was filed, had possession of the claimed invention.

1. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

2. "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

3. Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other

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cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

4. The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

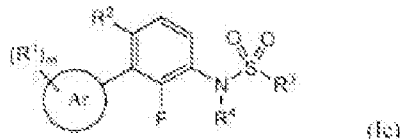
5. The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (i.e. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether

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applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph). Below is such comparison.

6. Scope of claims (elected invention):

I. (Original) A compound of formula (Ic):



or a pharmaceutically acceptable salt thereof,

wherein:

each R^1 is independently selected from optionally substituted lower alkyl or optionally substituted heteroaryl;

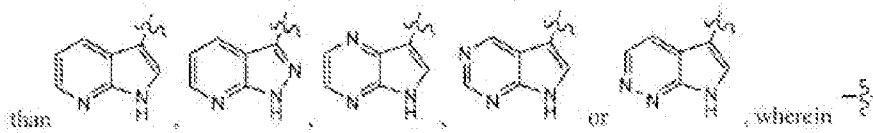
R^2 is hydrogen or halogen;

R^3 is optionally substituted aryl;

R^4 is hydrogen;

the subscript m is 2; and

Ar is optionally substituted heteroaryl, with the proviso that Ar is other



7. indicates the point of the attachment to the phenyl moiety in formula (Ic).

8. and pharmaceutical composition comprising the compound, pharmaceutical acceptable excipients, and additional active agents

9. **Scope of disclosure**

10. **Reduction to Practice**

The compounds reduced to practice support the following:

No compound within the claimed scope has been produced or disclosed, nor for their pharmaceutical property and utility.

11. Reduction to structural of chemical formulas:

11. The only disclosure, is in the form of general formula with lists of possible groups. See, Formula I, paragraph [0005] and formula Ic, paragraph [0015]. This kind of disclosure is not representation of any species. A "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species. MPEP 2163.1.A. and Fujikawa v. Wattanasin, 93 "3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed.Cir. 1996). Therefore, there is no species (e.g., by reduction to structural/chemical formulas) in addition to those reduced to practice.

12. Correlation between Structure and Function."

A correlation between structure and function, for the instantly claimed genus of compounds, is neither known in the art nor disclosed in the specification. All disclosed compounds have a linker moiety between the phenyl and the Ar. i.e., L1 in formula I is not a bond. The application provide no convincing evidence, or rationale that the biological activity of disclosed compounds would have been retained if the L1 in formula I is a bond instead of those linking moieties. Thus, it is not understood what specific structures for the claimed variables will lead to compounds that have the instantly claimed activity.

III. Analysis of Fulfillment of" Written Description Requirement:

The structure/activity relationship (SAR) for binding and activity is elucidated upon analysis of IC₅₀ data of multiple compounds with various types of structural modifications. These types of studies provide insight into the structural limitations that are required for activity, i.e. specific

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structural elements tolerated for the claimed activity. In the absence of such correlation, it is not possible to determine what structural modifications will allow for the preservation of the desired activity.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by claims 1, 2, 4-6, 8, 12-14 and 16-18; (ii) No disclosure of species supporting the genus; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

12. The following is a quotation of 35 U.S.C. 112(b):

(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-6, 8, 12-14 and 16-18 are rejected on the judicially-created basis that it contains an improper Markush grouping of alternatives. See *In re Harnisch*, 631 F.2d 716, 721-22 (CCPA 1980) and *Ex parte Hozumi*, 3 USPQ2d 1059, 1060 (Bd. Pat. App. & Int. 1984). The improper Markush grouping includes species of the claimed invention that do not share both a substantial structural feature and a common use that flows from the substantial structural feature.

The members of the improper Markush grouping do not share a substantial feature and/or a common use that flows from the substantial structural feature for the following reasons:

When the Markush grouping is for alternatives of chemical compounds, the alternatives are regarded as being of a similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity; AND

(B)(1) a common structure is present, that is, a significant structural element is shared by all of the alternatives; OR

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

The phrase “significant structural element is shared by all of the alternatives” refers to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity.

The phrase “recognized class of chemical compounds” means that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention, i.e. each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

In instant case, the claims read on numerous possible distinct species; there is no substantial structural feature shared by all species, the halogen and nitrogen substituted phenyl moiety is only a small portion of the complex structural herein. Such moiety is old and well - known in various compounds. see, e.g., WO 2007/002325, cited in the PCT report; and WO 2006/137376 (US 8067638 is an English equivalent, see, the abstract and the tables). Further, the compounds with distinct Ar moiety do not belong to a recognized class of chemical compounds, but in distinct classes in chemical/pharmaceutical art.

In response to this rejection, Applicant should either amend the claim(s) to recite only individual species or grouping of species that share a substantial structural feature as well as a

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common use that flows from the substantial structural feature, or present a sufficient showing that the species recited in the alternative of the claims(s) in fact share a substantial structural feature as well as a common use that flows from the substantial structural feature. This is a rejection on the merits and may be appealed to the Board of Patent Appeals and Interferences in accordance with 35 U.S.C. §134 and 37 CFR 41.31(a) (1) (emphasis provided).

This rejection may be overcome by amending the claims to include only the species that share a single structural similarity (i.e. Ar as defined in the elected species and R3 is phenyl).

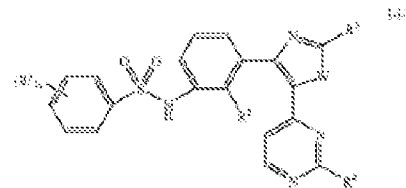
Claim Rejections 35 U.S.C. 103

13. The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 1, 2, 4-6, 8, 12-14 and 16-18 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Rheault (US 7,994,185, IDS) and Adjabeng et al. (US 8,415,345).

15. Note, '185 and '345 are in the same patent family having PCT publication of WO 2009/137,391 published on November 12, 2009.

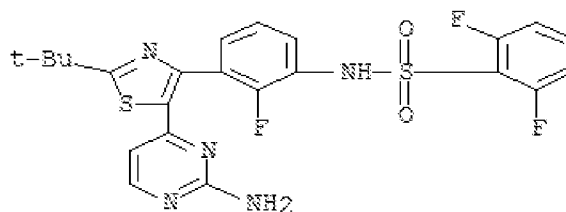


16. Rheault discloses compounds having a general formula

wherein a may be 0 to 2, R1 may be halo or alkyl, R2 may be halo, particularly, fluoro, R3 may

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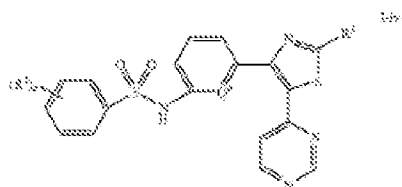
be alkyl, and R4 may be H, alkyl, or amino etc. See, particularly, columns 4-10. Expressly



disclosed examples includes,

(dabrafenib or GSK

2118436, compound claimed in claim 15).

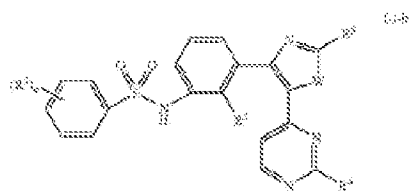


17. In one preferred embodiments, R4 is H:

, wherein Q4 is

C-R2. See, column 32. Compounds with a is 0 or R4 as hydrogen also been disclosed. See, e.g., columns 31, compound 219; column 317, compound 221. Adjabeng et al. (US 8,415,345) claims the compounds defined by the general formulae, pharmaceutical composition comprising the same, and method of using the same for treating melanoma. See, the claims.

18. The cited references do not teach expressly the compound elected herein, that is



wherein a is 0; R2 is F; R3 is methyl, and R4 is hydrogen.

However, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make the compound herein elected, and a pharmaceutical composition comprising the same and further with other known agents useful for treating melanoma.

A person of ordinary skill in the art would have been motivated to make the compound herein elected, and a pharmaceutical composition comprising the same and further with other known agents useful for treating melanoma because the cited references teach the general formula encompassing the compounds herein and provide examples for each of the substituents herein employed. The methyl group as R3 would have been obvious as the cited references teach that R3 may be alkyl, and provide examples with R3 as t-butyl or isopropyl. The employment of the methyl herein for substituting t-butyl or isopropyl is seen as to be a selection from amongst equally suitable material and as such obvious. Ex parte Winters 11 USPQ 2nd 1387 (at 1388). The further incorporation of other known active agent would have been obvious as it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for the very same purpose; idea of combining them flows logically from their having been individually taught in prior art. See In re Kerkhoven, 205 USPQ 1069.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

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applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1627