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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/494,978	07/28/2006	Volkmar Guenzler-Pukall	FP0600.3 CON	7438
41385	7590	07/23/2009		
FIBROGEN, INC. 409 Illinois Street San Francisco, CA 94158			EXAMINER JEAN-LOUIS, SAMIRA JM	
			ART UNIT	PAPER NUMBER
			1617	
			MAIL DATE	DELIVERY MODE
			07/23/2009	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.

<b>Office Action Summary</b>	<b>Application No.</b> 11/494,978	<b>Applicant(s)</b> GUENZLER-PUKALL ET AL.	
	<b>Examiner</b> SAMIRA JEAN-LOUIS	<b>Art Unit</b> 1617	

-- 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 13 April 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ 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

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 13-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ 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).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### 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).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
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 type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

**Election/Restrictions**

Claims 1-15 are currently pending in the application.

Applicant's election of Group I (i.e. method of stabilizing HIF-alpha), election of [(4-hydroxy-9-methyl-9H-beta-carboline-3-carbonyl)-amino]-acetic acid as the compound of formula Id, election of no additional therapeutic agent, and election of cardiac disorder in the reply filed on 04/13/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Thus, the requirement is deemed proper and is therefore made FINAL.

Claims 13-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Claims 1-12 are examined on the merits herein.

***Priority***

Acknowledgment is made of applicant's claim for domestic priority. It is noted, however, that applicant's elected species or subgenus encompassing such species is only recited in U.S. application 10/313,551 (hereinafter '551) filed December 06, 2002. Thus, the priority date of the instant invention is December 06, 2002. Therefore, art

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prior to the U.S. application '551 date, but not before the date of provisional application 60/337,082 filed December 06, 2001 may be cited against the claims.

### ***Provisional Non-Statutory Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

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be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5, and 7-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 9, 12-15, and 26 of copending Application No. 11/448,326 (hereinafter Klaus US Patent Application No. '326). Although the conflicting claims are not completely identical, they are not patentably distinct from each other because both applications are directed to a method of inhibiting hypoxia inducible factor alpha hydroxylase activity. The claimed invention and co-pending application Klaus '326 are rendered obvious over another as the claimed invention teaches a method of stabilizing HIF alpha by inhibiting hydroxylation of HIF alpha which necessarily occurs via inhibition of HIF hydroxylase activity whereas Klaus '326 teaches a method of treating anemia via inhibition of HIF hydroxylase activity. Consequently, both methods entail the same mechanistic pathway, i.e. inhibition of hydroxylase activity. Thus, the aforementioned claims of the instant application are substantially overlapping in scope as discussed hereinabove and are prima facie obvious over the cited claims of corresponding application No. 11/448,326.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making compounds of formula Id, does not reasonably provide enablement for making physiologically active salts or prodrugs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims are drawn to a method for stabilizing the alpha subunit of hypoxia inducible factor (HIF- $\alpha$ ) in a subject, the method comprising administering to the subject an amount of a compound of formula Id effective for inhibiting hydroxylation of HIF- $\alpha$  or a physiologically active salt or prodrug derived therefrom. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention.

Attention is directed to *In reWands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to a method for stabilizing the alpha subunit of hypoxia inducible factor (HIF- $\alpha$ ) in a subject, the method comprising administering to the subject an amount of a compound of formula Id effective for inhibiting hydroxylation of HIF- $\alpha$  or a physiologically active salt or prodrug derived therefrom. The relative skill of those in the art is high, that of a PHD. That factor is outweighed, however, by the unpredictable nature of the art. Specifically, the Examiner cites the fact that applicant has failed to demonstrate what compounds are prodrugs and what compounds are not and applicant fails to provide enablement support.

2. The breadth of the claims

The claims are thus very broad insofar as they recite a method for stabilizing the alpha subunit of hypoxia inducible factor (HIF- $\alpha$ ) in a subject, the method comprising

administering to the subject an amount of a compound of formula Id effective for inhibiting hydroxylation of HIF- $\alpha$  or a physiologically active salt or prodrug derived therefrom, yet applicant fails to provide enablement on the synthesis of the prodrugs of compounds of formula Id and how such synthesis will be accomplished.

2. The breadth of the claims

The claims are thus very broad insofar as they recite a method for stabilizing the alpha subunit of hypoxia inducible factor (HIF- $\alpha$ ) in a subject, the method comprising administering to the subject an amount of a compound of formula Id effective for inhibiting hydroxylation of HIF- $\alpha$  or a physiologically active salt or prodrug derived therefrom, yet applicant fails to provide enablement on the synthesis of the prodrugs and how such synthesis will be accomplished as previously mentioned.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification is not adequately enabled as to how to make a physiologically active salt and provides no direction or guidance for a method to synthesize the prodrugs of the aforementioned compounds. In fact, applicant discussed a single prodrug, pV but provided no structure for such compound or guidance on how to obtain such prodrug. As a result, countless experimentation would be necessary to obtain the prodrugs of the compounds of formula Id claimed by applicant.



4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed prodrugs could be predictably made as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation in order to obtain the prodrugs of the aforementioned compounds claimed by applicant, with no assurance of success.

Genentech, 108 F.3d at 1366 states that “ a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.”

Thus, in the absence of working examples there is no showing that one of ordinary skilled would immediately envisaged the instantly claimed prodrugs or their synthesis. Since it is clear that one of ordinary skill in the art would not readily envisaged what particular compounds are meant to be prodrugs, additional direction or guidance is needed to make them and the specification has no such direction or guidance. Therefore, only the chemically structurally defined chemicals, but not the full breadth of the claims meet the enablement requirement provision of 35 USC § 112, first paragraph.

Therefore, a method for a method for stabilizing the alpha subunit of hypoxia

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inducible factor (HIF- $\alpha$ ) in a subject, the method comprising administering to the subject an amount of a compound of formula Id effective for inhibiting hydroxylation of HIF- $\alpha$  or a physiologically active salt or prodrug derived therefrom is not considered to be enabled by the instant specification. However, for the sake of compact prosecution, the Examiner will construe that the compounds structurally derived from formula Id are enabled.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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.

Claims 1-12 are rejected under 35 U.S.C. 112, 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(s), at the time the application was filed, had possession of the claimed invention.

As stated by the court in Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), regarding the written description requirement:

The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.

In this instant application, applicant did not specifically describe compounds B and pV or the particular structures of such compounds in the specification (see specification (pg. 72, paragraphs 00172 and 00176, pg. 77, paragraph 00191 and figures 1-4). While applicant delineated the use of such compounds in conducting various experiments, applicant has failed to demonstrate the actual structures of such compounds and if indeed such compounds are encompassed by formula Id. This lack of written description thus renders it impossible for one skill in the art to envisage if such species are in fact encompassed by the aforementioned subgenus. Consequently, due to this lack of written description, the exact interpretation of the compounds of formula Id being claimed by applicant cannot be fully ascertained.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention (**see M.P.E.P 608.01 (k)**).

Claims 1-12 are particularly vague and indefinite given that applicant is claiming “physiologically active salts” (**in last sentence of claim 1**) and yet provides no clear definition as to what type of salts are considered a physiologically active salt. Given

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that applicant did not particularly point out what constitute a physiologically active salt or the properties that confer to a salt the characteristic of being physiologically active, one of ordinary skill in the art would not be able to fully ascertain the metes and bounds of the aforementioned claims.

As a result of the above inconsistencies, the aforementioned claims are unable to be examined as disclosed given that the scope of the claimed subject matter would not be able to be determined by one of ordinary skill in the art. However, for the sake of prosecution, the examiner will construe any pharmaceutical salt as a physiologically active salt.

### **Conclusion**

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th. 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.

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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 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). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L./

Examiner, Art Unit 1617

07/10/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617



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Volkmar Guenzler-Pukall

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FIBROGEN, INC.

409 Illinois Street

San Francisco, CA 94158

EXAMINER

JEAN-LOUIS, SAMIRA JM

ART UNIT

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

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<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	11/494,978	GUENZLER-PUKALL ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	SAMIRA JEAN-LOUIS	1627	

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#### Status

- 1) ☒ Responsive to communication(s) filed on 01 January 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ 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

- 4) ☒ Claim(s) 1-9 and 11-14 is/are pending in the application.
- 4a) Of the above claim(s) 13 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 11-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ 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).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### 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).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
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)

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| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Response to Arguments***

This Office Action is in response to the amendment submitted on 01/20/10. Claims 1-9 and 11-14 are currently pending in the application, with claims 10 and 15 having being cancelled and claims 13-14 having being withdrawn. Accordingly, claims 1-9 and 11-12 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

Applicant's traversal of the Obviousness Double Patenting (ODP) rejection of claims 1, 3-5, and 7-12 over claims 1-4, 9, 12-15, and 26 of copending application 11/448,326 is acknowledged, but since applicant did not put forth any arguments against this rejection, the ODP rejection was indeed proper. However, given that applicant has cancelled claim 10, a modified ODP rejection is made.

Applicant's argument with respect to the rejection of claims 1-12 under 35 U.S.C. 112, first paragraph has been fully considered. Given that applicant has amended the claims and deleted the terms "physiologically active salts" and "prodrugs", such rejection is now moot. Consequently, the rejection of claims 1-12 under 35 U.S.C. 112, first paragraph is hereby withdrawn.



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Applicant's argument with respect to the rejection of claims 1-12 under 35 U.S.C. 112, first paragraph has been fully considered. Applicant argues that compounds B and pV are not recited in claim 1 and are thus not relevant to the claims. Such arguments have been found persuasive as compounds B and pV do not fall under the generic formula Id. Consequently, the rejection of claims 1-12 under 35 U.S.C. 112, first paragraph is hereby withdrawn.

Applicant's argument with respect to the rejection of claims 1-12 under 35 U.S.C. 112, second paragraph has been fully considered. Given that applicant has amended the claims and deleted the terms "physiologically active salts" and "prodrugs", such rejection is now moot. Consequently, the rejection of claims 1-12 under 35 U.S.C. 112, second paragraph is hereby withdrawn.

For the foregoing reasons, the rejections of record are withdrawn. However, in view of applicant's amendment, the following modified ODP rejection and 112, first paragraph Non-Final rejection are being made.

### ***Provisional Non-Statutory Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

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A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5, 7-9, and 11-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 12-15, and 26 of copending Application No. 11/448,326 (hereinafter

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Klaus US Patent Application No. '326). Although the conflicting claims are not completely identical, they are not patentably distinct from each other because both applications are directed to a method involving the inhibition of hypoxia inducible factor hydroxylase activity. The claimed invention and co-pending application Klaus '326 are rendered obvious over another as the claimed invention teaches a method of stabilizing HIF alpha by inhibiting hydroxylation of HIF alpha which necessarily occurs via inhibition of HIF hydroxylase activity whereas Klaus '326 teaches a method of treating anemia via inhibition of HIF hydroxylase activity. Because both methods entail the same mechanistic pathway, i.e. inhibition of hydroxylase activity, such methods are not patentably distinct over another. Thus, the aforementioned claims of the instant application are substantially overlapping in scope as discussed hereinabove and are prima facie obvious over the cited claims of corresponding application No. 11/448,326.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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.

Claims 1-9 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for compounds of formula Id. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method for stabilizing the alpha subunit of hypoxia inducible factor (HIF- $\alpha$ ) in a subject, the method comprising administering to the subject an amount of a compound of formula Id effective for inhibiting HIF- $\alpha$  hydroxylase enzyme activity or a pharmaceutically acceptable salt derived therefrom. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention.

Attention is directed to *In reWands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

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1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to a method for stabilizing the alpha subunit of hypoxia inducible factor (HIF- $\alpha$ ) in a subject, the method comprising administering to the subject an amount of a compound of formula Id effective for inhibiting HIF- $\alpha$  hydroxylase enzyme activity or a pharmaceutically acceptable salt derived therefrom. The relative skill of those in the art is high, that of a PHD. That factor is outweighed, however, by the unpredictable nature of the art. Specifically, the Examiner cites the fact that applicant has failed to demonstrate how to use the compounds of formula Id and has thus failed to provide enablement support.

2. The breadth of the claims

The claims are thus very broad insofar as they recite a method for stabilizing the alpha subunit of hypoxia inducible factor (HIF- $\alpha$ ) in a subject, the method comprising administering to the subject an amount of a compound of formula Id effective for inhibiting HIF- $\alpha$  hydroxylase enzyme activity or a pharmaceutically acceptable salt derived therefrom, yet applicant fails to provide enablement on the use of the compounds of formula Id and if such usage is indeed predictive in stabilizing HIF- $\alpha$  as claimed by applicant.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance on how to use the compounds of formula Id in stabilizing HIF- $\alpha$  hydroxylase activity. While applicant tested several compounds for stabilization of the HIF- $\alpha$  protein, none of the compounds tested fell under the generic formula of Id. Because the tested compounds and the compounds of formula Id are structurally divergent, countless experimentation would be necessary to ascertain if the compounds of formula Id being claimed by applicant are indeed able to stabilize HIF- $\alpha$ .

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed compounds of formula Id could be predictably used to stabilize HIF- $\alpha$  as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation in order to use the aforementioned compounds claimed by applicant, with no assurance of success.

Genentech, 108 F.3d at 1366 states that “ a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.”

Thus, in the absence of working examples there is no showing that one of ordinary skilled would immediately accept that the instantly claimed compounds are in fact effective in stabilizing HIF- $\alpha$ . Since it is clear that one of ordinary skill in the art would not readily assert the compounds of formula Id can indeed stabilize HIF- $\alpha$  based on the evidence delineated in the present specification, additional direction or guidance is needed to use such compounds. Therefore, only the chemically structurally defined chemicals, but not the full breadth of the claims meet the enablement requirement provision of 35 USC § 112, first paragraph.

Therefore, a method for stabilizing the alpha subunit of hypoxia inducible factor (HIF- $\alpha$ ) in a subject, the method comprising administering to the subject an amount of a compound of formula Id effective for inhibiting HIF- $\alpha$  hydroxylase enzyme activity or a pharmaceutically acceptable salt derived therefrom is not considered to be enabled by the instant specification.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th. If attempts to reach the examiner by telephone are unsuccessful, the

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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.

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/S. J. L./

Examiner, Art Unit 1627

05/27/2010

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627