

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

U.S. SERIAL NO. : 12/928,119
APPLICANTS : Guenzler-Pukall, et al.
FILING DATE : 2 December 2010
GROUP ART UNIT : 1627
EXAMINER : Samira J.M. Jean-Louis
DOCKET NO. : FP0600.4 CON
TITLE : STABILIZATION OF HYPOXIA INDUCIBLE FACTOR (HIF) ALPHA

M/S: AMENDMENT
Commissioner for Patents
PO Box 1450
Alexandria VA 22313-1450

RESPONSE/AMENDMENT

Madam:

In response to the Office Action mailed 31 May 2012, the period for response being extended until 30 November 2012 by the accompanying petition and fee, please consider the above-identified application in view of the following amendments and remarks.

Amendments to the Claims are reflected in the listing of the claims, which begins on page 2 of this paper.

Remarks begin on page 3 of this paper.

AMENDMENTS
IN THE CLAIMS

The following is a complete listing of the claims in the application and replaces any prior listing of the claims.

Please cancel claim 9 without prejudice to renewal.

1. (Original) A method for treating tissue damage associated with hypoxia or ischemia in a subject, the method comprising administering to the subject an effective amount of a compound that stabilizes the alpha subunit of hypoxia inducible factor (HIF α).
2. (Original) The method of claim 1, wherein the compound is a heterocyclic carboxamide compound that inhibits HIF prolyl hydroxylase enzyme activity.
3. (Original) The method of claim 1, wherein the tissue damage is associated with an ischemic event.
4. (Original) The method of claim 3, wherein the ischemic event is acute.
5. (Original) The method of claim 3, wherein the ischemic event is associated with surgery, organ transplantation, infarction, trauma, or injury.
6. (Original) The method of claim 1, wherein the ischemia is chronic.
7. (Original) The method of claim 1, wherein the tissue damage is associated with ischemic reperfusion injury in a subject.
8. (Original) The method of claim 1, wherein the administering is oral administration.
9. (Canceled)

REMARKS

I. Claim status

Claims 1-9 were originally filed and were subject to a restriction requirement. Applicants elected the invention of Group I, claims 1-8, for examination. Claim 9 was subsequently withdrawn by the Examiner and is therefore canceled herein without prejudice to its renewal. Applicants specifically reserve the right to prosecute the subject matter of the canceled claim in continuing or divisional applications. Claims 1-8 are pending.

II. Information Disclosure Statement

Applicants appreciate Examiner's acknowledgement of the IDS submitted on 2 December 2010 and confirmation that the Examiner has considered and entered the IDS. Applicants respectfully request a copy of the submitted forms PTO/SB/08A and 08B indicating the citations considered by insertion of the Examiner's initials adjacent to each reference, or the phrase "[a]ll references considered except where lined through" along with the Examiner's electronic initials at the bottom of each page of the information disclosure statement, as stipulated at section 609.05(b) of the Manual of Patent Examining Procedure. Applicants request this copy to serve both as an acknowledgement of receipt of the information disclosure statement and as an indication as to which references were considered by the Examiner.

III. Priority

The present application is a continuation of U.S. Patent Application Serial No. 11/494,978, which is a continuation of U.S. application Serial No. 10/313,551, which claims the benefit of U.S. Provisional Patent Application Ser. No. 60/337,082, U.S. Provisional Patent Application Serial No. 60/359,683, U.S. Provisional Application Serial No. 60/349,659, and U.S. Provisional Patent Application Serial No. 60/386,488. The Examiner acknowledged Applicants' claim for the benefit of prior-filed applications, but stated that the earliest application providing adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. § 112 for the elected species in this application is U.S. Patent Application Serial No. 10/313,551, filed 6 December 2002. (Office Action, page 3.)

Applicants respectfully request reconsideration of this issue and draw the Examiner's attention in particular to U.S. Provisional Patent Application Serial No. 60/337,082 (the '082 application), filed

6 December 2001, and U.S. Provisional Patent Application Serial No. 60/359,683 (the '683 application), filed 25 February 2002.

The '082 application discloses compounds that stabilize HIF α and methods to treat conditions, diseases, or disorders associated with ischemia, including the tissue damage caused by an ischemic disorder. Treatment and prevention of tissue damage is specifically disclosed, e.g., on page 4, lines 19-21; and page 5, lines 1-5 and 10-11. The '082 application particularly recites "a compound of the invention can be used to prevent ischemic tissue injury" (page 5, line 1) and "as a pre-treatment to decrease or prevent tissue damage caused by an ischemic disorder" (page 5, line 10-11). The '082 application discloses compounds for use in the methods including the elected species in the present application. (See, e.g., page 6, lines 8-9.) The '082 application also provides examples demonstrating the ability of compounds to stabilize HIF α and treat tissue damage associated with hypoxia or ischemia in a subject. (See, e.g., Examples 1-4, 7, and 8.) The '082 application thus clearly provides support and enablement for the elected species in this application in the manner required by the first paragraph of 35 U.S.C. § 112. Accordingly, the instant invention is entitled the benefit of the priority date of the '082 application, 6 December 2001.

The '683 application also discloses compounds that stabilize HIF α and methods to treat conditions, diseases, or disorders associated with ischemia including the tissue damage caused by an ischemic disorder. Treatment and prevention of tissue damage is specifically disclosed, e.g., on page 4, lines 21-24; and page 5, lines 13-14 and 21-22. The '683 application particularly recites "a compound of the invention can be used to prevent tissue damage" (page 5, line 13) and "as a pre-treatment to decrease or prevent tissue damage" (page 5, line 21-22) caused by HIF-associated disorders including, but not limited to, ischemic disorders. The '683 application discloses compounds for use in the methods including the elected species in the present application. (See, e.g., page 6, lines 19-20.) The '683 application also provides examples demonstrating the ability of compounds including the elected species to stabilize HIF α and treat tissue damage associated with hypoxia or ischemia in a subject. (See, e.g., Examples 1-3, 5, and 6.) The '683 application thus clearly provides support and enablement for the elected species in this application in the manner required by the first paragraph of 35 U.S.C. § 112. Accordingly, the instant invention is entitled the benefit of the 25 February 2002 priority date of the '683 application.

In view of the above, the current claims being adequately supported and enabled in each of the priority documents discussed, the present application should be afforded the benefit of U.S. Provisional Patent

Application Serial No. 60/337,082, filed 6 December 2001, and should also be afforded the benefit of U.S. Provisional Patent Application Serial No. 60/359,683, filed 25 February 2002.

IV. Double Patenting

The Examiner provisionally rejected claims in the instant application on the ground of non-statutory obviousness-type double patenting in view of co-pending applications as outlined below:

1. Claims 1, 3, 4, 6, and 7 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-16 of co-pending U.S. Patent Application Serial No. 12/811,821 (the '821 application).
2. Claims 1 and 3-7 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-25 of co-pending U.S. Patent Application Serial No. 12/734,895 (the '895 application).
3. Claims 1 and 3-7 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 38-41 of co-pending U.S. Patent Application Serial No. 13/128,620 (the '620 application).
4. Claims 1 and 3-7 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-24 of co-pending U.S. Patent Application Serial No. 12/544,861 (the '861 application).

In each rejection, the Examiner stated that “the claimed invention teaches a subgenus of disease such as tissue damage utilizing a broad genus of compounds that stabilize HIF-alpha whereas [the co-pending application] teaches a broad genus of conditions to be treated utilizing a subgenus of compounds.” (See the Office Action, language corresponding to each of the '821, '895, '620, and '861 applications, at page 5, first paragraph; page 5, last paragraph; page 6, last paragraph; and 7, last paragraph, respectively.) The Examiner contended in each case that the present invention is obvious over the co-pending application “since the instant [invention] recites that the method is achieved by stabilizing HIF alpha and the co-pending [application] teaches that the method involves treatment of diseases mediated by HIF-alpha.” (Office Action, repeated for each rejection at page 5, first paragraph; page 5, last paragraph; page 6, last paragraph; and 7, last paragraph, respectively.) Applicants respectfully traverse each of these rejections.

The nonstatutory-type double patenting rejection is based on a judicially created doctrine grounded in public policy “which is primarily intended to prevent prolongation of the patent term by prohibiting

claims in a second patent not patentably distinguishing from claims in a first patent.” Manual of Patent Examining Procedure (MPEP) 804 (8th Edition, Revision 8). Nonstatutory double patenting includes rejections based on either a one-way determination of obviousness or a two-way determination of obviousness. In particular, “where, through no fault of the applicant, the claims in a later filed application issue first, an obvious-type double patenting rejection is improper, in the absence of a two-way obviousness determination....” MPEP 804(II)(B)(1)(b), citing *In re Braat*, 937 F.2d 589 (Fed.Cir 1991). “Under the two-way analysis, each claim is examined to determine whether it is an obvious variant of the other, rather than just examining the application claim for patentable distinctness from the patent claim.” *In re Emert*, 44 U.S.P.Q.2d 1149, 1152 (Fed. Cir. 1997).

In the present case, the instant application is earlier filed than any of the applications cited by the Examiner in the non-statutory obviousness-type double patenting rejections. The Examiner has acknowledged that the instant invention has the benefit of at least earlier filed Patent Application No. 10/313,551 (the ‘551 application), filed 6 December 2002 (Office Action, page 3), and the applications cited against the present claims have effective filing dates of about five years or more *after* the 6 December 2002 nonprovisional filing date of the ‘551 application. (The earliest claimed priority date for the ‘821 application is 11 January 2008; the earliest claimed priority date for the ‘895 application is 3 December 2007; the earliest claimed priority date for the ‘620 application is 14 November 2008; and the earliest claimed priority date for the ‘861 application is 20 August 2008.) Thus, the instant application is the earlier filed application, and the other applications cited by the Examiner are later filed applications.

Claim 1 of the present application recites “[a] method for treating tissue damage associated with hypoxia or ischemia in a subject, the method comprising administering to the subject an effective amount of a compound that stabilizes the alpha subunit of hypoxia inducible factor (HIF α).” Claims 3-7 depend directly or indirectly from claim 1. In the embodiment recited in claim 2, the “compound is a heterocyclic carboxamide compound that inhibits HIF prolyl hydroxylase enzyme activity.” Thus, the present application provides novel methods for treating tissue damage associated with hypoxia or ischemia using, generally, a compound that stabilizes HIF α , and, specifically, a heterocyclic carboxamide that inhibits HIF prolyl hydroxylase.

In contrast, each of the subsequently filed applications relates to specific subgenera of compounds that inhibit HIF hydroxylase enzyme activity, thereby increasing the stability and/or activity of hypoxia

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Applicants respectfully draw the Examiner's attention to *In re Borah*, 354 F.2d 1009 (CCPA 1966), in which an earlier filed but later allowed basic patent application was issued without a terminal disclaimer

as the improvements claimed in the later filed application were not made until after the application on the basic invention was filed. As in *Borah*, claims in the later filed '821 application, '895 application, '620 application, and '861 application could not have been filed in the instant application, at least in part because the later filed applications require the presence of an element not found in the instant claims to the basic invention, specifically the subgenera of novel compounds claimed in each of the later filed applications. Further, in *In re Braat*, the court applied the two-way test and reversed a non-statutory double patenting rejection because the later filed claims were patentably distinct from the earlier filed claims, even though the earlier filed claims were not patentably distinct from the later filed claims. *In re Braat*, 937 F.2d 589. As the subject matter of the claims in the '861, '895, '620, and '821 applications could not have been claimed in the earlier filed, present case, these later filed claims are also non-obvious over the instant claims. Therefore, the cited claims of the later filed applications are non-obvious over the instant invention, and the two-way obviousness test cannot be satisfied.

For at least the reasons provided above, claims 1, 3, 4, 6, and 7 of the present application are patentable over claims 13-16 of the later filed '821 application. Further, present claims 1 and 3-7 are patentable over claims 22-25 of the '895 application. Additionally, claims 1 and 3-7 are patentable over claims 38-41 of the '620 application and claims 2 -24 of the '861 application.

In view of the above, Applicants respectfully request withdrawal of the non-statutory double patenting rejection of these instant claims over the claims of the subsequently filed applications.

V. Rejections under 35 U.S.C. §112

Claims 1-8 were rejected under 35 U.S.C. § 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that claims 1-8 are "vague and indefinite given the applicant is claiming 'a compound that stabilizes the alpha subunit of hypoxia-inducible factor (HIFα)' while claim 2 recites "additional characteristics of what such compound may be but still only revealing minimal structural characteristics." (Office Action, page 8.) The Examiner further stated that, while the specification identified some compounds to be utilized, "the specification also states that other compounds are to be screened and identified to be utilized in the method of treatment," and that "one of ordinary skill would not be apprised of the structures of such compounds thereby rendering the metes and bounds of the recited compound vague and indefinite." (Office Action, page 8.) The Examiner also contended that the

disclosure “does not make clear what level of inhibition is required to satisfy the ‘inhibits’ language of the instant claims.” (Office Action, pages 8-9.) Applicants respectfully traverse.

The Examiner stated that claims 1-8 are unclear because one of skill would not be apprised of the structure of compound recited in the claims and would not know the level of inhibition required to satisfy the “inhibits” limitation of the claims. The test for definiteness under 35 U.S.C. §112, 2nd paragraph, is whether “those skilled in the art would understand what is claimed when the claim is read in light of the specification.” *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576 (Fed. Cir. 1986) (citations omitted).

Claim 1 recites “[a] method for treating tissue damage associated with hypoxia or ischemia in a subject, the method comprising administering to the subject an effective amount of a compound that stabilizes the alpha subunit of hypoxia inducible factor (HIF α).” The specification provides both general guidelines (e.g., paragraphs [0133] to [0136]) and specific examples (e.g., Examples 1, 3-5, and 9) for determining whether a compound stabilizes HIF α . The specification describes tests as applied to various compounds and provides clear guidance regarding the requisite degree to which a compound may “inhibit” in order to be encompassed by the claim; see, e.g., data presented in Figures 1A, 1B, 2A, 2B, 4A, 4B, 5A, 5B, 6A, and 6B. The recitation in claim 1 provides a clear cut indication of the scope of the subject matter covered by the claim and sets forth well-defined boundaries of the invention. Accordingly, those skilled in the art would understand what is claimed when claim 1 is read in light of the specification.

Claims 2-8, which depend directly or indirectly from claim 1, are not indefinite for at least the reasons provided above for claim 1. Additionally, claim 2 recites the compound “is a heterocyclic carboxamide that inhibits HIF prolyl hydroxylase enzyme activity.” Heterocyclic carboxamides are well-known to those skilled in the art, and one of ordinary skill would know from this claim term what structures are encompassed by the claims. The specification further provides examples of heterocyclic carboxamides that inhibit HIF prolyl hydroxylase enzyme activity and thereby stabilize HIF α . (See, e.g., Example 10.) Thus, one of skill in the art would clearly understand what is claimed when the claims are read in light of the specification.

As evidenced by the above, those skilled in the art would understand what is claimed in claims 1-8 when the claims are read in light of the specification. For at least these reasons, claims 1-8 are clear and definite. Therefore, Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §112, 2nd paragraph, as being indefinite.

VI. Rejections under 35 U.S.C. § 103

Claims 1-8 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Maxwell et al. (International Publication No. WO 02/074981). The Examiner stated that “one of ordinary skill in the art at the time of the invention would have found it obvious to administer the compounds of Maxell [sic] that modulate the activity of HIF α through inhibition of HIF hydroxylase since Maxell [sic] teaches that such compounds are effective for tissue damage due to ischemic events.” (Office Action, page 12.)

Applicants respectfully traverse.

Maxwell et al. was published on 26 September 2002 from a PCT application filed on 21 March 2002. As Applicants point out in section III above, Provisional Patent Application Serial No. 60/337,082, filed 6 December 2001, and Provisional Patent Application Serial No. 60/359,683, filed 25 February 2002, provide support and enablement in the manner required by the first paragraph of 35 U.S.C. §112 for the instant claims 1-8, including support and enablement for the elected species in this application. Accordingly, the instant invention should be granted the benefit of the priority date of the '082 application, that is, 6 December 2001, and the priority date of the '683 application, that is, 25 February 2002. As either date is prior to Maxwell's earliest filing date of 21 March 2002 or publication date of 26 September 2002, Maxwell et al. is therefore not prior art against the present invention.

As Maxwell et al. is not prior art against the present invention for at least the reasons provided above, Applicants respectfully request withdrawal of the rejection of claims 1-8 under 35 U.S.C. §103(a) as being unpatentable over Maxwell et al.

CONCLUSION

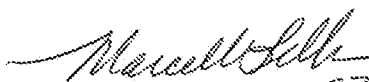
Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended above is respectfully requested.

Applicants claim small entity status under 37 C.F.R. 1.27.

The Commissioner is hereby authorized to charge the total of any fee necessary in this communication to Deposit Account No. 50-0811, referencing Docket No. FP0600.4 CON.

Please call Applicants' representative at 415-978-1745 with any questions regarding the present communication or the above-identified application.

Respectfully submitted,


REG. NO. 36,583

Date: 29 Nov 2012

By: 

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