IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Jerome B. Zeldis	Group Art Unit: 1618
Application No.: 13/070,761	Confirmation No.: 2735
Filed: March 24, 2011	Examiner: Samala, Jagadishwar Rao
For: METHODS OF TREATING MYELODYSPLASTIC SYNDROMES USING LENALIDOMIDE (as amended)	Attorney Docket No.: 12827-089-999 (CAM 226269-999089)

RESPONSE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In response to the non-final Office Action mailed May 9, 2012, Applicant respectfully submits the following remarks for consideration by the Examiner and entry into the record of the above-identified application. Also submitted herewith is a Petition for Extension of Time for one month from August 9, 2012 to and including September 10, 2012 (September 9, 2012 being a Sunday).

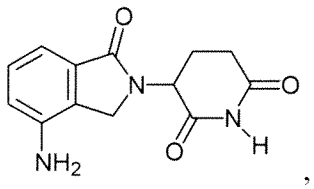
A listing of the claims begins on page 2 of this paper.

Remarks begin on page 4 of this paper.

Listing of the Claims:

1-37. (canceled)

38. (Previously Presented) A method of treating a patient having transfusion dependent anemia due to low to intermediate -1- risk myelodysplastic syndrome, which comprises administering to said patient about 5 to about 25 mg per day of 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione having the formula:



or a pharmaceutically acceptable salt, solvate or stereoisomer thereof.

39. (Previously Presented) The method of claim 38, wherein the compound is administered in the amount of 5 mg per day.

40. (Previously Presented) The method of claim 38, wherein the compound is administered in the amount of 10 mg per day.

41. (Previously Presented) The method of claim 38, wherein the compound is administered in the amount of 15 mg per day.

42. (Previously Presented) The method of claim 38, wherein the compound is administered in the amount of 25 mg per day.

43. (Previously Presented) The method of claim 39, wherein the compound is administered orally in an amount of 5 mg as a capsule per day.

44. (Previously Presented) The method of claim 40, wherein the compound is administered orally in an amount of 10 mg as a capsule per day.

45. (Previously Presented) The method of claim 41, wherein the compound is administered orally in an amount of 15 mg as a capsule per day.

46. (Previously Presented) The method of claim 42, wherein the compound is administered orally in an amount of 25 mg as a capsule per day.

47. (Previously Presented) The method of claim 43, 44, 45 or 46, wherein the compound 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione is as a free base.

REMARKS

Claims 38-47 are pending in the application. Reconsideration of the pending claims in view of the remarks below is respectfully requested.

I. Claim Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

Claims 38-47 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Pellegrino *et al.* (*Haematologica* 87(8): 884-886, August 2002) in view Muller *et al.* (U.S. Patent No. 5,635,517). The Examiner states that Pellegrino discloses a method of treating transfusion-dependent patients with myelodysplastic syndrome (MDS) by administering thalidomide. (Office Action at 3). The Examiner acknowledges that Pellegrino does not teach the compound 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione recited in the instant claims, but asserts that Muller discloses a method of administering thalidomide analogs for reducing undesirable levels of tumor necrosis factor α (TNF-α), and that the formula for the thalidomide analogs in Muller would read on the instant compound. *Id.* Based on these, the Examiner alleges that it would have been obvious to one of ordinary skill in the art to incorporate the 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione into Pellegrino's composition. (*Id.* at 4). For the following reasons, Applicant respectfully disagrees with this rejection.

Claim 38 recites a method of treating a patient having transfusion dependent anemia due to low to intermediate -1- risk myelodysplastic syndrome, comprising administering about 5 to about 25 mg per day of 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione (hereafter referred to as "lenalidomide"). Claims 39-47 depend on claim 38 directly or indirectly, and therefore incorporate all of its elements. Thus, the claimed methods do not require incorporating lenalidomide into Pellegrino's composition, as the PTO alleged. Office Action at 4.

Applicant respectfully points out that the Examiner bears the burden of establishing a case of *prima facie* obviousness against the claims as a whole. That is, all the claim elements must be considered in a 103 rejection and the Examiner must show how the references render such obviousness. *In re Royka*, 490 F.2d 81 (CCPA 1974). Here, the cited references would not

have provided any reason for one of skill in the art specifically to select administering the specific compound lenalidomide for treating a patient having transfusion dependent anemia due to low to intermediate -1- risk myelodysplastic syndrome, much less the claimed methods using the specific amounts and specific dosing regimens.

Pellegrino studied the efficacy of thalidomide on transfusion-dependent patients with MDS. Twenty-five (25) patients were enrolled in the study. Nine of the twenty-five patients have a low score under the international prognostic system, thirteen patients have an intermediate 1-2 score, and three patients have a high score. (*See* Pellegrino, page 884, 2nd col., 1st para.). Thalidomide was administered at the dose of 100 mg/d per os for one week to test tolerance, and then was progressively increased every four weeks up to 300 mg/d. *Id.* Twenty patients stopped the treatment due to either side effects or inefficacy. The remaining five patients became transfusion-free. (*Id.* at 2nd col., 2nd para.). It should be noted that the doses of thalidomide given to these five responsive patients were between 200 mg/d and 300 mg/d. (*See* table 1).

Pellegrino solely focuses on the efficacy of thalidomide and does not disclose or suggest the use of any other agent such as a thalidomide analog for treating patients with MDS, much less the specific compound recited in the instant claims, *i.e.*, 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione. Moreover, Pellegrino does not disclose or suggest the dosage amount recited in the pending claims, which is from about 5 to about 25 mg per day. In fact, since the five patients that responded to the treatment each received at least 200 mg/d of thalidomide up to 300 mg/d, Applicant submits that Pellegrino teaches away from the claimed method. Prior art is said to teach away from a claimed invention "[w]hen a piece of prior art 'suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant....'" *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006) (quoting *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994)) (emphasis added); *see also KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (citing *United States v. Adams*, 383 U.S. 39, 40 (1966)); MPEP § 2145 (citing *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983)).

Muller does not remedy the deficiencies of Pellegrino. Muller discloses that certain amino-substituted isoindolines reduce the levels of TNF-a in a mammal and that decreasing

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