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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Jerome B. Zeldis	Confirmation No.:	9157
Serial No.:	10/411,649	Art Unit:	1614
Filed:	April 11, 2003	Examiner:	Kim, Vickie Y
For:	METHODS OF USING 3-(4-AMINO-1-OXO-1,3-DIHYDRO-ISOINDOL-2-YL)-PIPERIDINE-2,6-DIONE FOR THE TREATMENT AND MANAGEMENT OF MYELODYSPLASTIC SYNDROMES	Attorney Dkt No.:	9516-072-999 (CAM: 501872-999071)

AMENDMENT, STATEMENT OF INTERVIEW SUMMARY AND RESPONSE

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

Sir:

In response to Final Office Action dated March 30, 2006, please consider and enter the amendments and remarks provided below into the file of the above-captioned application. Submitted herewith are a Request for Continued Examination and Supplemental Information Disclosure Statement, each with the provision for the required fees.

Amendment to the Title begins on page 2 of this response.

Amendments to the Specification are reflected in the listing of claims that begins on page 3 of this paper.

Amendments to the Claims are reflected in the listing of the claims that begins on page 4 of this paper.

Remarks begin on page 8 of this paper.

Amendment to the Title:

Please amend the title of the application as follows:

METHODS OF USING ~~IMMUNOMODULATORY COMPOUNDS~~ 3-(4-AMINO-1-OXO-1,3-DIHYDRO-ISOINDOL-2-YL)-PIPERIDINE-2,6-DIONE FOR THE TREATMENT AND MANAGEMENT OF MYELODYSPLASTIC SYNDROMES

Amendments to the Specification:

Please replace the third paragraph on page 33 with the following amended paragraph:

In vitro studies suggest a pharmacological activity profile for 3-(4-amino-1-oxo- 1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione that is similar to, but 50 to 2000 times more potent than, thalidomide. The pharmacological effects of 3-(4-amino-1-oxo-1,3-dihydro- isoindol-2-yl)-piperidine-2,6-dione derive from its action as an inhibitor of cellular response to receptor-initiated trophic signals (*e.g.*, IGF-1, VEGF, cyclooxygenase-2), and other activities. As a result, 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione suppresses the generation of inflammatory cytokines, down-regulates adhesion molecules and apoptosis inhibitory proteins (*e.g.*, cFLIP, cIAP), promotes sensitivity to death-receptor initiated programmed cell death, and suppresses angiogenic response. The studies show that 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione abrogates mitogenic response to VEGF in AML cells by extinguishing ligant-induced Akt-phosphorylation, and selectively suppresses MDS vs normal bone marrow progenitor formation in pre-clinical models.

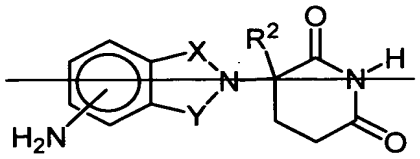
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of the Claims:

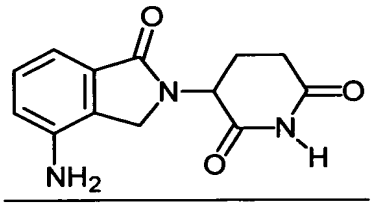
Claims 1-38 (canceled).

39. (currently amended) A method of treating a myelodysplastic syndrome, which comprises administering to a patient in need thereof ~~a therapeutically effective amount of a compound of formula (I):~~



~~(I)~~

about 5 to about 50 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~~, wherein one of X and Y is C=O, the other of X and Y is C=O or CH_2, and R^2 is hydrogen or lower alkyl having 1 to 4 carbon atoms~~.

40-41. (canceled.)

42. (previously presented) The method of claim 39, wherein the compound is a pharmaceutically acceptable salt.

43. (previously presented) The method of claim 39, wherein the compound is a pharmaceutically acceptable solvate.

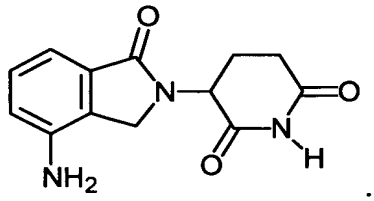
44. (previously presented) The method of claim 39, wherein the compound is a pharmaceutically acceptable stereoisomer.

45. (previously presented) The method of claim 44, wherein the stereoisomer is an enantiomerically pure R isomer.

46. (previously presented) The method of claim 44, wherein the stereoisomer is an enantiomerically pure S isomer.

47 (canceled).

48. (previously presented) The method of claim 39, wherein the compound is 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione having the formula:



49. (previously presented) The method of claim 39, which further comprises administering a therapeutically effective amount of a second active agent.

50. (previously presented) The method of claim 49, the second active agent is capable of improving blood cell production.

51. (previously presented) The method of claim 49, wherein the second active agent is a cytokine, hematopoietic growth factor, an anti-cancer agent, an antibiotic, a proteasome inhibitor, or an immunosuppressive agent.

52. (previously presented) The method of claim 51, wherein the second active agent is etanercept, imatinib, anti-TNF-α antibodies, infliximab, G-CSF, GM-CSF, EPO, topotecan, pentoxifylline, ciprofloxacin, irinotecan, vinblastine, dexamethasone, IL2, IL8, IL18, Ara-C, vinorelbine, isotretinoin, 13-cis-retinoic acid, arsenic trioxide or a pharmacologically active mutant or derivative thereof.

53. (previously presented) The method of claim 39, wherein the myelodysplastic syndrome is refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, or chronic myelomonocytic leukemia.

54. (previously presented) The method of claim 39, wherein the compound or a pharmaceutically acceptable salt, solvate or stereoisomer thereof is administered before, during or after transplanting umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in the patient.

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