Docket No.: PIR-88501
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
John C. Byrd, *et al.*

Application No.: 14/523,650 | Confirmation No.: 1095

Filed: October 24, 2014 | Art Unit: 1629

For: METHODS OF TREATING AND PREVENTING GRAFT VERSUS HOST DISEASE | Examiner: TRAN, My Chau T.

AMENDMENT AND RESPONSE

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

Dear Sir:

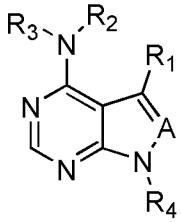
In response to the pending Office Action, dated April 22, 2016, in connection with the above-referenced application, Applicant submits this Response. Please amend the application as follows.

Amendments to the Claims begin on page 2.

Remarks begin on page 6.

IN THE CLAIMS:

1. (Currently amended) A method of treating ~~preventing the occurrence of~~ graft versus host disease (GVHD), or reducing the severity of GVHD occurrence, in a patient having chronic GVHD ~~requiring cell transplantation~~, comprising administering to the patient a therapeutically effective amount of a compound of Formula (A) having the structure:



Formula (A);

wherein:

A is N;

R_1 is phenyl-O-phenyl or phenyl-S-phenyl;

R_2 and R_3 are independently H;

R_4 is L_3-X-L_4-G, wherein,

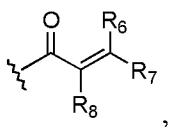
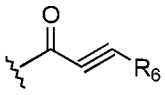
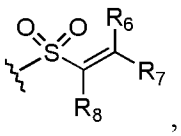
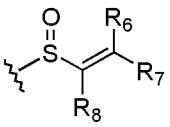
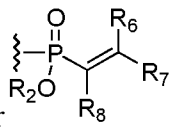
L_3 is optional, and when present is a bond, optionally substituted or unsubstituted alkyl, optionally substituted or unsubstituted cycloalkyl, optionally substituted or unsubstituted alkenyl, optionally substituted or unsubstituted alkynyl;

X is optional, and when present is a bond, -O-, -C(=O)-, -S-, -S(=O)-, -S(=O)$_2$-, -NH-, -NR$_9$-, -NHC(O)-, -C(O)NH-, -NR$_9$C(O)-, -C(O)NR$_9$-, -S(=O)$_2$NH-, -NHS(=O)$_2$-, -S(=O)$_2$NR$_9$-, -NR$_9$S(=O)$_2$-, -OC(O)NH-, -NHC(O)O-, -OC(O)NR$_9$-, -NR$_9$C(O)O-, -CH=NO-, -ON=CH-, -NR$_{10}$C(O)NR$_{10}$-, heteroaryl-, aryl-, -NR$_{10}$C(=NR$_{11}$)NR$_{10}$-, -NR$_{10}$C(=NR$_{11}$)-, -C(=NR$_{11}$)NR$_{10}$-, -OC(=NR$_{11}$)-, or -C(=NR$_{11}$)O-;

L_4 is optional, and when present is a bond, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl,

substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocycle;

or L_3, X and L_4 taken together form a nitrogen containing heterocyclic ring;

G is  ,  ,  ,  , or  , wherein,

R_6, R_7 and R_8 are independently selected from among H, halogen, CN, OH, substituted or unsubstituted alkyl or substituted or unsubstituted heteroalkyl or substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

each R_9 is independently selected from among H, substituted or unsubstituted lower alkyl, and substituted or unsubstituted lower cycloalkyl;

each R_{10} is independently H, substituted or unsubstituted lower alkyl, or substituted or unsubstituted lower cycloalkyl; or

two R_{10} groups can together form a 5-, 6-, 7-, or 8-membered heterocyclic ring; or

R_{10} and R_{11} can together form a 5-, 6-, 7-, or 8-membered heterocyclic ring; or

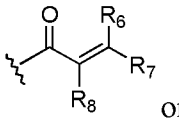
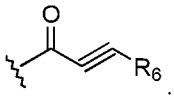
each R_{11} is independently selected from H or substituted or unsubstituted alkyl; or a pharmaceutically acceptable salt thereof,

thereby treating the~~preventing the occurrence of~~ graft versus host disease (GVHD) or reducing the severity of GVHD occurrence in the patient.

2. (Canceled)

3. (Original) The method of claim 1, wherein L_3, X and L_4 taken together form a nitrogen containing heterocyclic ring.

4. (Original) The method of claim 3, wherein the nitrogen containing heterocyclic ring is a piperidine group.

5. (Original) The method of claim 1, wherein G is  or  .

6. (Original) The method of claim 1, wherein the compound of Formula (A) is 1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidin-1-yl]prop-2-en-1-one.

7. (Currently amended) The method of claim 1, wherein the chronic GVHD is sclerodermatous GVHD, steroid resistant GVHD, cyclosporin-resistant GVHD, refractory GVHD, oral GVHD, ~~chronic~~ oral GVHD, reticular oral GVHD, erosive GVHD, or ulcerative oral GVHD.

8. (Currently amended) The method of claim 1, wherein the chronic GVHD is sclerodermatous GVHD.

9. (Currently amended) The method of claim 1, wherein the chronic GVHD is steroid resistant GVHD.

10. (Original) The method of claim 1, wherein the patient has chronic lymphocytic leukemia (CLL).

11. (Currently amended) The method of claim 1, wherein the patient had ~~cell transplantation is~~ a hematopoietic cell transplantation.

12. (Canceled)

13. (Canceled)

14. (Canceled)

15. (Original) The method of claim 1, wherein the compound of Formula (A) is administered at a dosage of between about 0.1 mg/kg per day to about 100 mg/kg per day.

16. (Currently amended) The method of claim 1, wherein the amount of the compound of Formula (A) administered is about 40 mg/day, about 140 mg/day, about 280 mg/day, about 420 mg/day, about 560 mg/day, or about 840 mg/day.

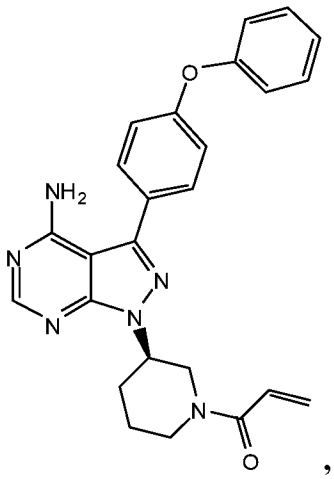
17. (Canceled)

18. (Original) The method of claim 1, wherein the compound of Formula (A) is administered orally.

19. (Withdrawn) The method of claim 1, wherein the compound of Formula (A) is administered in combination with one or more additional therapeutic agents.

20. (Withdrawn) The method of claim 19, wherein the additional therapeutic agent is a corticosteroid, cyclosporine (CSA), mycophenolate mofetil (MMF), or a combination thereof.

21. (New) A method of treating chronic graft versus host disease (GVHD) comprising administering to a patient having chronic GVHD a therapeutically effective amount of a compound of the structure:



,

or a pharmaceutically acceptable salt thereof.

22. (New) The method of claim 21, wherein the patient has classic chronic GVHD.

23. (New) The method of claim 21, wherein the patient has overlap chronic GVHD.

24. (New) The method of claim 21, wherein the patient has steroid-dependent/refractory chronic GVHD.

25. (New) The method of claim 21, wherein the therapeutically effective amount of the compound is about 40 mg/day, about 140 mg/day, about 280 mg/day, about 420 mg/day, about 560 mg/day, or about 840 mg/day.

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